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AETIOLOGICAL ASPECTS OF MULTIPLE SCLEROSIS

BY

HENRY MILLER, M.D., F.R.C.P. *Physician* AND KURT SCHAPIRA,* M.B. *Research Fellow*

From the Neurological Department, Royal Victoria Infirmary, and the Department of Medicine, the Medical School, King's College, Newcastle upon Tyne

PART I

Although a hundred and twenty years of phenomenal advance in medicine have passed since multiple sclerosis was first described, we remain ignorant not only of its cause but even of its general nature. Is this because it is due to an entirely new kind of causal agent, as yet unthought-of? Is some as yet unidentified agent belonging to a known category responsible? Or does the disease depend on some unusual combination of pathogenetic factors already familiar? That multiple sclerosis will yield its secrets to a merely heuristic approach is unlikely, but the crucial observations or experiments which ultimately elucidate its nature may well originate in some speculation.

In few diseases can we recognize the operation of a single "cause" such as the genetic anomaly of Huntington's chorea or the typhoid bacillus, and we are increasingly reconciled to thinking in terms of multiple aetiological factors of differing valency, and of extended disease processes involving a complex succession of patho-physiological mechanisms, rather than of frozen "disease-entities." Such an approach, while discomfiting to the tidy-minded, has the advantage that it permits the isolation of various stages in the disease process as appropriate subjects both for investigation and for therapeutic intervention. After all, truly aetiological information about peptic ulcer remains sketchy, but fragmentary knowledge of its pathogenesis has furnished the theoretical basis for various forms of effective treatment.

The history of aetiological theories in multiple sclerosis throws as much light on the development of medical thought in general as on the nature of the disorder. Carswell (1838) and Cruveilhier (1829–42), who first described the condition, respectively attributed the plaques of the disease to ischaemia, and the disorder in general to the suppression of "insensible perspiration." Early histopathological observers such as Rindfleisch (1863) and Moxon (1875) stressed the inflammatory and perivascular nature of early lesions, and Leyden (1863) postulated the aetiological role of non-specific incidents such as acute illness, trauma, exposure, and emotional disturbance—factors enumerated unchanged in the text-books of to-day. Charcot (1868, 1872) supported Moxon in implicating infectious diseases as a causal factor: that such a relationship was consistent and central to the problem of aetiology was first postulated by Pierre Marie (1895), and accepted by many, including Gowers (1893). However, on the basis of one of the earliest personal series of cases reported, Krafft-Ebing (1895) regarded body-chilling as more significant, while Strümpell (1896) envisaged the role of an inborn vulnerability of the nervous system. The latter view appealed to Bramwell (1917), who sought to combine it with the hypothesis of "auto-intoxication," on which Dawson (1916) had speculated in his unequalled pathological study.

The last fifty years have seen the unsuccessful search for a specific infective agent which has revolved chiefly round the spirochaete and the virus. Even allowing for its notoriously elusive nature, evidence incriminating the former is frankly unconvincing. The question of a viral aetiology for multiple sclerosis has been reviewed by Innes and Kurland (1952): there is no positive evidence in its favour, nor does the evidence preclude such a possibility.

Acute Disseminated Encephalomyelitis

Glanzmann's (1927) study of the acute disseminated (perivenous demyelinating) encephalomyelitic syndromes which occasionally complicate measles and Jennerian vaccination opened a new chapter of speculation and investigation into the aetiology of multiple sclerosis, and it is to this aspect of the problem that the present paper is chiefly addressed. Obscure though the exact pathogenesis of these rare disorders might be, they possessed the signal advantage as objects of study and comparison that each such illness was the outcome of a single identifiable aetiological event. Furthermore, it was soon established that whether the encephalomyelitis was caused by measles, chicken-pox, influenza, vaccination, or merely a non-specific respiratory infection, the characteristic pathological lesion encountered was the same, suggesting the intervention of some common pathogenetic factor between the varied initial insult and the uniform sequel; in this connexion Glanzmann speculatively invoked von Pirquet's (1907) concept of allergy.

The clinical and pathological similarities of these syndromes to acute episodes of multiple sclerosis were soon appreciated, and as early as 1928 Pette described three cases exhibiting a gradient of pathological changes progressing from acute perivenous demyelinating encephalitis to a more subacute syndrome of four months' duration with marginal gliosis which he interpreted as an unequivocal instance of the chronic disease.

The relationship between acute disseminated encephalomyelitis and multiple sclerosis is still debated.

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McAlpine (1931) drew attention to the frequency in encephalomyelitis of certain symptoms such as clouding of consciousness, meningism, high fever, severe limb pains, and radicular lesions with flaccid palsy and areflexia; and to the rarity of other clinical features such as euphoria, unilateral retrobulbar neuritis, and diplopia, which are often encountered in multiple sclerosis. Recovery from a frankly post-infective lesion such as transverse myelitis has also been widely regarded as usually more rapid and more complete than from a comparable episode of the chronic disease. However, an appreciable proportion of cases originally diagnosed as encephalomyelitic have subsequently declared themselves to have been initial episodes of multiple sclerosis.

Opponents of Pette's unitary view who conceded the symptomatic overlap between the two syndromes claimed that the subsequent history of patients with acute disseminated encephalomyelitis established the condition as a clinical entity independent of the chronic disease. That the two conditions could hardly be regarded as identical was supported by the observation that out of a total of 75 such cases followed up by Thygesen (1949), van Bogaert (1950), and Miller and Evans (1953), no fewer than 42 showed no recurrence of neurological symptoms over a period of years. Furthermore, even when relapse or recurrence did occur in encephalomyelitic cases, the progressive disability associated with strangulation of the long tracts by massive fibrous gliosis characteristic of chronic multiple sclerosis was lacking. This last observation can, however, hardly be regarded as more than tautological: any case in which chronic disability of this kind followed an encephalomyelitic illness would almost certainly be omitted from such a series by hindsight as an instance of multiple sclerosis.

Histopathology

Histopathological differentiation is similarly controversial, such studies being hampered especially by the infrequency of death during an acute exacerbation of unequivocal multiple sclerosis: many of the earlier cases so described prior to 1927 would generally be regarded to-day as instances of acute disseminated encephalomyelitis. It is, however, now widely accepted that, while the characteristic plaques of chronic multiple sclerosis show no consistent relationship to vascular territories, the initial lesion of the disease is usually if not always perivascular, and very similar in nature to that of the encephalomyelitic syndrome. The main difference appears to be that, while perivascular cuffing and demyelination following measles or vaccination are generalized and uniform, the similar changes in multiple sclerosis are essentially focal, and the cuffing intermittent along the course of the vessels. Such a difference might, for instance, be regarded as analogous to that seen in the field of systemic disease between the solitary generalized exudative explosion of acute serum sickness and the localized chronic lesions of polyarteritis nodosa, which appear to be due either to repeated exogenous antigenic insults or to the initiation of some self-perpetuating process of iso-immunization such as has recently been demonstrated in thyroid disease.

It is not difficult to equate the more global encephalomyelitic lesion with the greater frequency of symptoms indicating generalized involvement of the neuraxis, such as clouding of consciousness and symmetrical involvement of optic nerves, long tracts of the spinal cord, and nerve-roots—in contrast to the characteristic clinical asymmetry of early multiple sclerosis. Such a statement must be qualified by the observation that the polymorphic symptomatology of encephalomyelitis itself indicates that the apparent pathological uniformity is far from absolute, and that this difference is probably one of degree. Somewhat similar though less acute pathological changes are encountered at the margins of chronic plaques, a finding which has led some authorities to suggest that, despite its episodic clinical manifestations, the pathological course of multiple sclerosis may nevertheless be insidious rather than intermittently explosive.

The most untiring advocate of the unitarian view that the disease represents in its pathological essence nothing more than a chronic recurrent disseminated encephalomyelitis of allergic origin is Ferraro (1937, 1944, 1958), who regards the chronic plaques as the result of coalescence of multiple acute perivenous foci, and glial scarring as merely the outcome of relapses causing repeated damage to areas previously involved.

Most patients who die of acute disseminated encephalomyelitis do so within a few days of its onset, and histopathological evidence is scanty regarding the changes found in patients who recover or who have survived for longer periods. *Complete resolution* of the acute changes has been recorded, though both *coalescent demyelination* (Herkenrath, 1935; Schaltenbrand, 1938) and *extensive gliosis* (Schlesinger, 1909; van Bogaert, 1932) have occasionally followed such an illness.

Experimental Allergic Encephalomyelitis

The demonstration that a perivenous demyelinating encephalomyelitis widely accepted as analogous to the human post-infective syndrome discussed above can be regularly provoked in animals by repeated injections of sterile brain emulsion, and that its development can be effectively inhibited by the prior administration of corticotrophin, has clinched the fact that this lesion can arise *independently of infection*, and has lent strong support to its allergic origin.

To have induced acute disseminated encephalomyelitis in animals is not, however, to have reproduced multiple sclerosis, and these important observations have thrown no new light on the crucial problem of the relationship between these acute self-limited clinical and experimental syndromes on the one hand and the relapsing self-perpetuating course of the chronic human disease on the other.

Neurological Sequelae of Rabies Vaccination

In this connexion, however, important evidence has recently been furnished from Japan by Uchimura and Shiraki (1957), who describe the findings in nine patients dying after subacute neurological illnesses which followed preventive inoculation against rabies—a form of human prophylaxis which closely parallels the animal experiments noted above, in that it involves repeated injections of heat-treated animal neural tissue. Their illustrations show widespread massive demyelinated lesions, clear-cut, often closely related to the ventricular margins, and characterized by marked gliosis; it can hardly be doubted that these represent a later evolution by confluence of the perivascular foci found in earlier cases, which appear entirely similar to those familiar in the more commonly encountered forms of acute disseminated encephalomyelitis. The unique iatrogenic illnesses from which these patients suffered were of

subacute encephalomyelitic type, and not classical multiple sclerosis. The significance of these observations is pathological: they present human lesions of known aetiology (and almost certainly allergic pathogenesis) which are more strikingly similar to those of multiple sclerosis and Schilder's disease (diffuse sclerosis) than anything previously described.

Some Clinical Considerations

Any current hypothesis on the aetiology of multiple sclerosis must be compatible with certain established facts in the natural history of the disease. In relation to its age incidence we would merely record that we have encountered its acute onset in classical form at all ages between 6 and 60 years.

Differing standards of medicine preclude a comprehensive view of geographical incidence, but the disease is commoner in the northern than in the southern hemisphere, and in the northern than in the southern parts of the former. We do not know whether this greater prevalence in cold climates is related, as has been suggested, to a higher incidence either of infections of the upper respiratory tract or of vasospastic disorders, nor whether removal to warmer conditions would protect patients against recurrence as it does in rheumatic fever.

Implications of a Genetic Factor

The fact that a second patient with multiple sclerosis is found in the families of between 6 and 7% of cases (McAlpine, 1957) has been taken to imply a genetic factor in the production of the disease: if so it is remarkable that recent investigations (Pratt, 1951; Thums, 1951; Mackay and Myrianthopoulos, 1957) have conspicuously failed to show any significant degree of concordance in the occurrence of multiple sclerosis in monozygotic twins. In the most recent of these observations, Mackay and Myrianthopoulos reported 27 instances of the disease in one identical twin, and in 21 of these the other was unaffected. The situation is even further complicated by the fact that other members of such families show an incidence of multiple sclerosis strikingly in excess of that encountered in the general population. We have encountered one such instance in our unpublished series of more than 600 cases of multiple sclerosis personally examined in the course of a regional survey.

Case 493.—In 1948, at the age of 36, a woman, one of nine sibs, developed sudden diplopia. In April, 1954, she became unsteady and weak on her legs, and was found to have typical signs of mild multiple sclerosis with nystagmus, pallor of the disks, and an asymmetrical ataxic paraplegia. Re-examination in 1958 revealed more gross signs, with marked cerebellar ataxia of all limbs and a spastic quadriparesis, in addition to advanced bilateral optic atrophy with nystagmus. Her 46-year-old *identical twin* was also examined at this time, ten years after the onset of the patient's illness. At no time had the twin sister suffered any neurological symptoms, and physical examination of the nervous system was completely normal. The identical nature of the twinship was established by serial photographs and blood-grouping. However, *another sister* (Case 418), born in 1918, six years after these twins, developed classical multiple sclerosis in March, 1955, with gross ataxia and loss of vision in the right eye, diplopia, and nystagmus. The spinal fluid at this time showed a paretic Lange curve, and the diagnosis of multiple sclerosis was confirmed by rapid recovery from this episode and by a relapse with loss of proprioceptive sensation in the right arm and leg in February, 1958. A *fourth sib*, born in 1901 (not accepted in our survey as an authenticated case of multiple sclerosis), suffered from acute unilateral retrobulbar neuritis in 1936, but has remained well since. Five other sibs, including another pair of heterozygotic twins, were normal with regard both to history and to neurological examination, but a *paternal cousin* born in 1901 developed an acute paraplegic syndrome in 1935 and exhibited classical signs of advanced multiple sclerosis on re-examination in 1958.

On the other hand, the rarity of conjugal cases militates equally against a contagious explanation of the familial incidence.

The occasional evident influence of one of a number of non-specific factors (trauma, exposure, fatigue, infection, and probably emotional disturbance) in provoking the onset or exacerbation of multiple sclerosis is strongly supported by clinical evidence not necessarily invalid because it is drawn from individual cases. This evidence is indeed so suggestive that it remains impressive in spite of the fact that no such relationship is consistently encountered, and that in many cases none whatever can be traced. The cause of these well-authenticated phenomena remains obscure: some kind of reflex circulatory disturbance seems to be the most plausible guess at a common factor.

Relationship with Trauma

On the face of it, for example, an aetiological relationship between trauma and multiple sclerosis appears unlikely. There is, however, a group of cases in which not only a temporal but also a topographic relationship to injury is so striking that such a connexion can be denied only in the light of preconceived notions which are themselves of dubious validity in the light of recent observations on the traumatic provocation and localization of paralytic poliomyelitis.

Case 501.—In March, 1958, a 23-year-old dental student was struck on the left cheek by a hockey ball. A large haematoma developed below the zygoma and there was a good deal of pain in the cheek and the inside of the mouth. This pain gradually cleared, but the haematoma was still present six days after the injury, when he developed numbness and tingling over the left cheek. This spread rapidly to the palate and the inside of the lower jaw, and involved the whole of the left trigeminal distribution within 24 hours of its onset. In view of the haematoma, and although there was no radiological evidence of fracture, this condition was thought possibly to be traumatic until three days later, when he developed similar tingling in the right arm and leg. Signs of local injury cleared up within two weeks, but it was five weeks before his neurological symptoms disappeared. Six weeks later he developed a typical episode of acute disseminated sclerosis with ataxic nystagmus, diplopia, and a right hemiparesis. Again disability on this score cleared rapidly, and the only abnormal findings four weeks later were absence of the abdominal responses and an extensor plantar response on the right side, with minimal nystagmus.

Case 453.—In November, 1954, a 47-year-old man sustained an extensive superficial electrical burn to his left hand, and within six days of this he noticed an abnormal sensation of numbness in the hand and half-way up the forearm. When the dressing was removed the limb was found to be clumsy, and within a few days the numbness spread to the left face and leg, and also to the tips of the fingers of the right hand. The only abnormal finding at this stage was a left hemihypaesthesia, which included the face. Diagnosis was obscure, but a tentative suspicion of multiple sclerosis was confirmed by the development in 1957 of fatigability and unsteadiness of gait, when examination revealed ataxia, sustained vertical nystagmus, right lower facial weakness, left intention tremor, absent abdominal reflexes, a right plantar response, and patchy

impairment of sensation over the left side of the body. With the exception of spinal fluid examination, which showed a marked rise in gamma-globulin content, all ancillary investigations were negative.

The sensory nature of the initial post-traumatic symptoms in these cases is worthy of note: signs of initial involvement of afferent pathways from the affected part have characterized other such cases in the literature.

Non-specific Infections

Non-specific infections have gradually replaced the epidemic fevers of the nineteenth century as putative aetiological factors in multiple sclerosis, but in fact clinically evident infection of any kind is often entirely lacking in the recent history of early cases. Although Abb and Schaltenbrand (1956) claim to have traced it in more than two-fifths of patients, the figures given by most other workers are much lower. Störtebecker's (1951) claim to have revealed a high incidence of miscellaneous antecedent infections in cases of multiple sclerosis by means of agglutination, antistreptolysin, and antistaphylolysin titres is suggestive, but as yet unconfirmed. Nor — although reliable figures are entirely lacking—has the gradual conquest of the bacterial infections during the past two decades been followed by any apparent decline in the frequency of new cases of multiple sclerosis comparable with that of which we cannot fail to be aware in the case of such frankly post-infective disorders as acute rheumatism or acute nephritis.

Again, occasional cases are impressive.

Case 90.—In December, 1949, a 26-year-old woman developed a severe head cold with fever and influenzal symptoms, followed within 24 hours by the sudden appearance of a partial transverse spinal-cord lesion at the mid-dorsal level. This improved rapidly after a few days, and 10 weeks later there was no residual disability. During the next seven years she had six similar episodes, each involving the spinal cord at the same level, always in winter and always immediately preceded by a frank and sometimes febrile upper respiratory infection. The three later episodes also involved the arms, and one of these was accompanied by double vision and one by pronounced left hemiparesis. Each attack lasted for less than 12 weeks, and each cleared up, leaving minimal disability. The only other episode was in the summer of 1952, when she had an attack of nystagmus and double vision lasting for two weeks, quite unrelated to clinically evident infection. Examination in 1957 revealed a mild spastic paraparesis with appropriate reflex changes. Astereognosis was found in both hands, and vibration sense was lost in the left hand and leg.

Allergy

Much the same reservations apply to the role of allergy, reviewed by Prigal (1956). Occasional cases are striking in which frank allergic disturbance appears to have provoked the onset or exacerbation of the disease (Compston, 1951), but statistics are unimpressive. However, anamnestic investigation of allergy is mainly limited to obtaining evidence of its more striking manifestations, such as atopy, of which evidence may be entirely lacking in other diseases which we know to arise on an allergic basis. The observations of Alexander *et al.* (1950) that multiple sclerotics show an incidence of transfusion reactions (mostly allergic) thirty times as great as that encountered in control cases is suggestive clinical evidence in favour of some instability in the machinery of immunity in these cases, while the demonstration of a frequent increase in the spinal fluid gamma-globulin (Kabat *et al.*, 1942; Yahr *et al.*, 1954) and of an abnormal response to the intrathecal injection of tuberculin (Smith *et al.*, 1957) have been similarly interpreted. The significance of these last findings, however, remains obscure: they may represent secondary results of the vascular and meningeal changes of the disease rather than evidence of a primarily immunological disturbance.

[The conclusion of this article, together with a list of references, will appear in our next issue.]

THE ARTIFICIAL KIDNEY

BY

F. M. PARSONS, M.B., Ch.B., B.Sc.

Assistant Director, Metabolic Disturbances in Surgery, M.R.C. Unit, Leeds

AND

B. H. McCRACKEN, M.D., B.Sc., M.R.C.P.

Lecturer in Medicine, University of Leeds

(From the General Infirmary at Leeds)

Severe renal failure is evidenced clinically by the syndrome of uraemia. This is believed to be due to the accumulation in the body of a number of substances, only a few of which have probably been identified. The artificial kidney is a device for removing from the body some or all of these substances. Various types of machine have been used for this purpose, and their historical development has been reviewed by Merrill (1955) and by Sorrentino (1956). All of them have employed the principle of dialysis, using a semi-permeable membrane that separates a bathing solution from the patient's blood.

Dialysis with any type of artificial kidney is a complicated and time-consuming procedure, and its greatest therapeutic value has been in the treatment of patients with acute reversible renal failure.* It has also been used for the treatment of patients with exacerbation of chronic renal failure (Parsons and McCracken, 1957) and barbiturate (Kyle, Jeghers, Walsh, Doolan, Wishinsky, and Pallotta, 1953) and other acute poisonings (Doolan, Walsh, Kyle, and Wishinsky, 1951; Danzig, 1955; Merrill and Weller, 1952). It has a limited use in maintaining life in order that diagnostic procedures can be undertaken in patients presenting with the more obscure types of renal failure. The artificial kidney also provides an opportunity of obtaining information about the uraemic state, and its potentialities as a research tool are largely unexplored.

Following the pioneer work of Kolff and Berk (1944), reports of experience with artificial kidneys have appeared chiefly from the U.S.A. (Skeggs and Leonards, 1948; Merrill, 1950; Kolff, 1957), Scandinavia (Alwall, 1947; Anthonisen, Brun, Crone, Lassen, Munck, and Thomsen, 1956; Thaysen, Gjørup, and Killmann, 1957), and the mainland of Europe (Legrain, 1953; Hamburger and Richet, 1956). Use of the apparatus in Great Britain prior to 1956 has been confined to its occasional employment between 1947 and 1949 (Bull, Joekes, and Lowe, 1958); since 1956 machines have been in use in two centres, and preliminary reports of these have been

*The term "acute reversible renal failure" is used in preference to others, such as lower nephron nephrosis, tubular necrosis, etc.

published (Parsons and McCracken, 1957; Shackman and Milne, 1957). The present paper gives an account of 20 months' experience with the artificial kidney in Leeds.

Description of the Machine

We have used the Kolff rotating type of machine as modified at the Peter Bent Brigham Hospital, Boston. A full account of this has been given by Murphy, Swan, Walter, Weller, and Merrill (1952). A diagram of the essential parts is shown in Fig. 1.

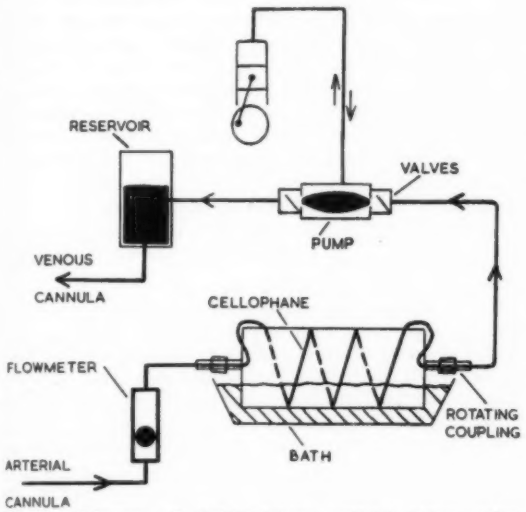

FIG. 1.—Diagram of Kolff-Brigham artificial kidney (after Merrill, 1955). Reproduced by permission of the Editor of the *British Journal of Urology*.

We have introduced certain modifications to this machine. The rate of blood flow through the dialyser has been increased from 300 ml. a minute to a maximum of 550 ml. a minute, and the dialysing surface area of the "cellophane" has been increased from 21,000 to 28,000 sq. cm. These alterations have improved the clearance rates of both urea and creatinine by approximately 40% (Parsons and McCracken, 1958a).

The composition of the bath fluid has been modified by using the acetates of calcium, magnesium, and potassium in place of chlorides (Table I). This prevents the occurrence of hyperchloraemia during the dialysis and results in a more complete correction of the plasma bicarbonate level. The acetates of calcium and magnesium have another advantage; for, unlike the chloride, they are not hygroscopic, so that they can be stored ready for use in the solid state. It has been emphasized previously that the concentration of sodium in the bath fluid should be the same as that in the patient's plasma (Parsons and McCracken, 1957). This is achieved by varying the quantity of sodium chloride added to the bath fluid.

TABLE I.—*Typical Composition of Bath Fluid. The Upper Half Gives the Weight of Chemicals Added to 100 Litres, and the Lower Half the Ionic Strength*

$NaCl^*$	660 g.	Ca acetate	20 g.
$NaHCO_3$	225 g.	Mg acetate $4H_2O$	10·4 g.
K acetate	34·3 g.	Glucose	400 g.
Leeds tap-water	100 litres		
Na^*	140 mEq/l.	Mg	1·7 mg. per 100 ml.
K	3·6 "	Ca	6 "
HCO_3	27 "	Cl^*	113 mEq/l."

* Adjusted according to plasma level of Na.

We also dialyse the citrated blood used to prime the machine. This partly corrects the high citrate and low calcium levels in the plasma of the citrated blood before it reaches the patient's circulation (Parsons and McCracken, 1958a). This has virtually eliminated the incidence of reactions developing at the start of the dialysis.

The Procedure

The dialysis, which is carried out in a special room, is continued for six hours, but the whole procedure takes about nine hours. Two pints (1,140 ml.) of stored blood, less than 5 days old, are required to fill the machine prior to use, and, to prevent clotting, a total of 14,000 units of heparin is given intravenously in divided doses during the dialysis.

A trained team of four persons, consisting of medical and nursing staff, is necessary for the dialysis, and a chemical laboratory service is often required. The procedure is not unduly trying to the patient, and sedation should be avoided, if possible, as it frequently causes lowering of the blood pressure in the advanced uraemic state.

Origin of Patients

100 patients were referred for treatment on the artificial kidney, and 82 required dialysis. (We have excluded from this series seven patients in a terminal phase of chronic nephritis who were treated soon after receiving the machine.) The 100 patients are classified in Table II. Twenty-four of them were referred to us from Leeds and 76 came from the Midlands, Northern England, and South-west Scotland.

Acute Renal Failure.—(1) *Reversible:* 63 patients with acute reversible renal failure were treated—25 cases occurred as a complication of pregnancy, 25 as a result of or associated with trauma, and 13 from other causes.

TABLE II.—*Classification of the 100 Treated Patients*

	No. Treated	No. Dialysed
Acute renal failure:		
Reversible — Pregnancy	25	17
Reversible — Trauma	25	19
Reversible — Others	13	9
Irreversible	13	13
Post-renal obstruction:		
Reversible	9	9
Irreversible	4	4
Miscellaneous	11	11

(2) *Irreversible:* 13 patients were admitted with acute renal failure and required a dialysis. Subsequently they were found to have an irreversible disease. Five had acute glomerulosclerosis, two had necrotizing arteriolitis, two had bilateral cortical necrosis of pregnancy, one had generalized amyloid disease involving the kidneys, one had acute diffuse glomerulonephritis, one had subacute diffuse glomerulonephritis, and one had acute suppurative pyelonephritis of one kidney, the other kidney being congenitally absent. These patients are not discussed further in this communication.

Post-renal Obstruction.—(1) *Reversible:* Nine patients were dialysed who had post-renal obstruction and uraemia due to disorders subsequently amenable to surgery. (2) *Irreversible:* Four patients were treated with the artificial kidney. Three presented with anuria, and a retrograde pyelogram revealed a bilateral ureteric obstruction. In two of these patients a periureteric fibrosis was suspected, and the dialysis prepared the patient for a nephrostomy; but a biopsy, taken from the site of obstruction, revealed unsuspected malignant

disease. The third patient was found to have carcinomatosis at a laparotomy. The fourth patient had a recurrent carcinoma of the cervix invading the posterior wall of the bladder. These patients are not discussed further.

Miscellaneous.—This group concerns the remaining 11 patients who were treated with the artificial kidney. Nine had an exacerbation of chronic renal disease, and five recovered. We have treated too few of this type of patient to draw justifiable conclusions, and consider, for the time being, that each patient has to be judged separately. The remaining two patients in this group had no renal failure. One was in diabetic coma and survived. The other had a fulminating acute hepatic coma, but the dialysis made no apparent difference to the clinical condition, and he died two days later. These 11 patients are not discussed further.

Clinical Management

The clinical management of all patients referred to the Artificial Kidney Unit has been our direct responsibility. All the patients, whether medical, surgical, obstetrical, or gynaecological, have normally been admitted to one male or one female ward. Daily records of the patients' weight, blood pressure, fluid balance, and blood chemistry are kept.

Acute Reversible Renal Failure.—The fluid intake was restricted to the amount necessary to achieve a daily weight loss of 300–400 g. In anuric patients this is usually achieved with a fluid intake of 400 ml. a day. Calories were limited to the amount contained in 100–200 g. of glucose, and a generous vitamin intake is given. The glucose, water, and vitamins were given by mouth, for, so far as was possible, we avoided both intragastric and intravenous therapy. Electrolyte administration was restricted to replacement of losses in urine, stool, or vomit, and the occasional use of sodium lactate as an emergency procedure in patients with severe acidosis or hyperkalaemia. Cation exchange resins were used to control hyperkalaemia only when the rise in potassium was out of proportion to the other chemical indices of uraemia. When the renal function returns to the extent of causing a fall in the blood urea nitrogen (B.U.N.), restrictions on food intake are removed, and full protein feeding is encouraged as soon as it is tolerated. Electrolyte supplements are given at this time as required, and fluid intake is determined by the volume of urine and previous fluid requirements, except in patients with frank overhydration in whom fluid intake has been curtailed until the excess water has been eliminated. Dialyses were performed when considered necessary, but this did not affect the basic therapeutic regime.

Acute Irreversible Renal Failure.—This group (Table II) mainly concerns patients who presented as diagnostic problems, there being no definite antecedent episode heralding the onset of renal failure. They received the same dietary management as the previous group, and dialyses were performed when thought necessary. In addition diagnostic procedures, such as bilateral retrograde pyelography, and percutaneous or open renal biopsy, were carried out. When an irreversible condition was found the dietary restrictions were relaxed and no further dialyses were performed.

Post-renal Obstructions. — As a major surgical procedure causes an increase in metabolic rate (Moore and Ball, 1952), we have used dialysis to correct a uraemic state prior to surgical intervention. In patients with prostatic obstruction whose uraemic state has not been corrected by catheterization, we have used the artificial kidney early, and then waited for renal function to improve before performing a prostatectomy. This not only allows us to correct malnutrition in these patients before operation, but also prevents the occurrence of uraemia in the immediate post-operative period, when the heparinization necessary for haemodialysis might lead to excessive haemorrhage from the prostatic bed. Following the relief of a chronic post-renal obstruction many patients lose excessive amounts of sodium chloride in the urine, and ionic supplementation is required even during the immediate post-operative period (Parsons, 1954). This salt loss is usually temporary. After a dialysis there is often a reduction in urinary output in these patients, and we usually adjust the fluid intake to maintain a constant body weight. The taking of protein is encouraged, the quantity being adjusted to the degree of renal failure.

Clinical Effects of Dialysis

The clinical improvements achieved by dialysis are usually delayed for 24 to 48 hours. The immediate responses that occur during dialysis are chiefly cardiovascular—any arrhythmias due to potassium intoxication are corrected within 15 minutes, and uraemic hypotension is usually rectified in two to four hours. When uraemic twitching and mental agitation are present they tend to be temporarily aggravated rather than improved during the period of dialysis, and in two instances thiopentone had to be administered intravenously to control convulsions. During the 48 hours following dialysis, nausea and vomiting are replaced by hunger, and normal cerebration is restored. Acidotic breathing, if present, usually disappears within 12 hours. These improvements are maintained for several days even in the presence of severe oliguria. Anaemia gradually increases in severity, and we have not observed any rise in the level of haemoglobin following a dialysis. Normal haemopoiesis is restored only when renal function has returned. Concentrated red blood cells have been used to raise the haemoglobin level when this has been necessary.

Chemical Effect of Dialysis

The chemical response is mainly immediate and is greatly influenced by the efficiency of the machine. This is dependent on many factors, such as the initial concentration of substances in the plasma, the volume of distribution of these substances in the body, the duration of the dialysis, the properties of the dialysing membrane, the rate of blood flow through the dialyser, and the accumulation of substances in the bath. These aspects have been discussed elsewhere (Parsons and McCracken, 1958a).

A typical chemical response obtained by the Kolff-Brigham dialyser is shown in Table III. This patient

TABLE III.—*Chemical Response to Dialysis and the Findings 48 Hours Later*

Plasma Levels	Start of Dialysis	End of 6 Hours' Dialysis	48 Hours Later
Na (mEq/l.)	133	135	144
Cl	91·5	101	100
CO_2 c.p. mEq/l.	14·8	27·2	23·1
K mEq/l.	6·4	4·1	5·1
P (mg./100 ml.)	15·3	2·1	10·4
B.U.N.	200	31	66
*p*H (arterial blood) ..	7·23	7·49	—

developed an acute renal failure following an abortion, and was dialysed on the 11th day. As her plasma level of sodium was 133 mEq/l. the composition of the bath was adjusted to contain 135 mEq/l., and the plasma level of sodium rose to 135 mEq/l. during the dialysis. The level of chloride, CO_2 combining power, potassium, and B.U.N. returned to more normal values. The plasma inorganic phosphorus level fell to 2.1 mg./100 ml., at the conclusion of the dialysis, but 48 hours later it was 10.4 mg./100 ml., a rise out of proportion to the increase in the B.U.N. (Parsons and McCracken, 1957). During the dialysis the *p*H in the arterial blood rose from 7.23 to 7.49. This over-correction of arterial *p*H during the dialysis was reported by Weller, Swan, and Merrill (1953), but we have found that it returns to normal values some hours after the dialysis. Similarly the low partial pressure of CO_2 in the alveolar air at the start of the dialysis remains unaltered during the procedure, but some hours after the dialysis it returns to normal values (Ramwell, Parsons, and McCracken, 1959). In anuria or severe oliguria a gradual return to the pre-existing chemical state occurs after the dialysis (Table III).

Complications During a Dialysis

Artificial Kidney. — The Kolff–Brigham machine requires constant supervision during the dialysis. Mechanical faults have been few and have been limited to those parts carrying the blood. They can usually be rectified by substituting a sterilized spare component or length of P.V.C. tubing. The most frequent fault was the presence of a hole in the cellophane tube, and this can be rectified by replacing the affected area with a short length of plastic tubing as described by Merrill, Thorn, Walter, Callahan, and Smith (1950). The working blood volume of our machine is 1 to 1.5 litres, but as the potential capacity is approximately 8 litres it is essential to guard against large fluctuations of blood in the machine, as these can only occur at the expense of the corporeal circulation. In three patients the dialysis had to be terminated as the blood clotted in the machine. In the first a slow flow rate was responsible. The second patient had generalized amyloid disease and the heparin had probably been adsorbed by the amyloid deposits. The third patient had received severe traumatic injuries six days previously, but later three further dialyses were performed and no clotting occurred.

Patient.—Serious complications occurring in the patient are infrequent. No fatalities have been directly attributable to a dialysis, though three patients died during the procedure. Two were in advanced uraemic coma ; the third had had an operation for aortic stenosis, and an acute cardiac arrest developed 30 minutes after starting the second dialysis. We have had to terminate the dialysis five times on account of complications—three for haemorrhage in post-operative wounds, one for an exacerbation of a mental disturbance, and one for the development of a small cerebrovascular accident. None of these complications proved fatal.

Results in Acute Reversible Renal Failure

Pregnancy: Dialysed

Seventeen patients were treated by dialysis, and all recovered. The findings of these patients are summarized in Table IV. Twelve developed acute renal failure associated with complications occurring in late pregnancy and five had abortions. Eight patients required a dialysis during the 5th to 7th days, six during the 8th to 10th days, and three were dialysed after the 10th day. Four required more than one dialysis.

At the time of dialysis all exhibited clinical deterioration, the commonest feature being deterioration of the mental state and nausea or vomiting. The blood chemistry at the time of the dialysis (Table IV) revealed that the B.U.N. exceeded 180 mg./100 ml. in nine patients. In only four was the plasma potassium level greater than 7 mEq/l., and in only four was the CO_2 combining power less than 14 mEq/l.

We measured the average daily rise in the B.U.N. in 15 patients who were observed over a sufficiently long period of severe oliguria to draw a justifiable conclusion. In two the rise was less than 15 mg./100 ml., in 12 the rise was between 15 and 30 mg., and in one it exceeded 30 mg.

The earliest fall in the B.U.N. occurred on the 12th day (Cases 42 and 57), whilst in only four was the fall delayed longer than the 25th day. The fall in the B.U.N. occurred most commonly about five days after the urine output exceeded 500 ml. per 24 hours. The average time taken before the B.U.N. started to fall in these 17 patients was 20 days. The maximum urinary output per day during recovery was not high, and averaged 2,700 ml. (range 771–5,025 ml.). Ten of these patients were discharged before the 40th day after the onset of renal failure, and the remaining seven stayed in hospital longer, either because their period of oliguria was prolonged or because complications had occurred.

Pregnancy: Non-dialysed

Eight patients were treated without a dialysis (Table V) and six recovered. One of the patients died 30 minutes after admission and the other died in uraemia as we failed to dialyse early enough. In this patient (Case 1 N) the B.U.N. a few hours before death was 181 mg./100 ml., and the potassium level of the plasma was 6.6 mEq/l. (a level of 9.0 mEq/l. had been lowered by means of ion-exchange resins eight days earlier).

Of the six patients who recovered, three had abortions, and three had complications occurring in late pregnancy. None of these patients developed a severe acidosis or hyperkalaemia, and the highest B.U.N. recorded was 168 mg./100 ml. (Case 3 N). The clinical condition of these patients remained good throughout the period of oliguria.

The B.U.N. fell earlier than in the previous group, the fall occurring on days 3 to 17, whilst the average maximum urinary output was similar, being 2,740 ml. per 24 hours. These patients were discharged earlier than those who were dialysed, mainly because the period of oliguria was much shorter.

Trauma: Dialysed

Nineteen patients who developed acute renal failure as a result of trauma or of association with trauma have been dialysed and six recovered. The findings on these patients are summarized in Table IV. Five of these patients had received accidental trauma (three survived) and 14 (three survived) had had a major surgical operation.

In the main, the first dialysis had to be performed early in the course of the illness. Nine patients were dialysed on or before the 5th day, four on the 5th to 7th days, four on the 8th and 10th days, and only two after

TABLE IV.—*Findings in Patients who were Dialysed for Acute Reversible Renal Failure*

Cause	Case No.	Age and Sex	Day Transfer to Kidney Unit	1st Dialysis after Admission Days	No. of Dialyses	Plasma Levels at First Dialysis			Average Daily Rise of B.U.N. mg./100 ml.	Day Urine Output Exceeded 500 ml./24 Hours	Day 1st Fall in B.U.N.	Maximum Urine Output ml./24 Hours	Outcome
						K mEq/l.	CO_2 c.p. mEq/l.	B.U.N. mg./100 ml.					
Pregnancy Group													
Abortion	9	39 F	5	2	1	5·1	15·2	120	17·5	13	20	2,800 34th day	Discharged 37th day
Accidental haemorrhage	12	39 F	8	<1	3	8·8	13·5	216	22·6	19	35	3,000 44th day	Discharged 59th day
Abortion	18	31 F	6	2	2	5·5	10·5	118	12·8	26	31	2,930 45th day	Discharged 50th day
Haemorrhage; placenta praevia	28	29 F	4	3	1	5·7	15·4	216	36	9	14	3,120 14th day	Discharged 45th day
Pre-eclampsia	31	25 F	20	<1	1	2·8	19·1	320	—	>500 on admission	27	3,600 40th day	Discharged 41st day
Abortion	33	33 F	2	7	1	4·8	14·8	178	15	11	17	2,760 20th day	Discharged 36th day
"	35	24 F	7	4	1	6·6	14·8	200	13·5	13	19	2,345 18th day	Discharged 25th day
Toxaemia of pregnancy	36	31 F	2	3	3	6·8	16·1	146	16·3	38	42	771 51st day	Discharged 68th day
Eclampsia	42	26 F	6	<1	1	8·4	14·8	176	15	8	12	2,910 14th day	Discharged 23rd day
Accidental haemorrhage	43	35 F	7	<1	2	6·4	14·8	250	27·5	13	18	2,520 18th day	Discharged 25th day
Abortion with hysterectomy	54	27 F	6	<1	1	4·5	15·5	188	19·5	13	14	3,000 30th day	Discharged 40th day
Accidental haemorrhage	55	21 F	8	<1	1	5·9	13·6	174	20	15	16	2,145 26th day	Discharged 29th day
Toxaemia of pregnancy	57	27 F	3	3	1	7·1	15·2	190	15	6	12	5,025 12th day	Discharged 20th day
Accidental haemorrhage	67	39 F	6	2	1	6·0	16·4	204	20	17	19	2,525 23rd day	Discharged 36th day
Toxaemia of pregnancy	76	32 F	13	2	1	5·8	9·6	144	—	20	24	1,890 39th day	Discharged 47th day
Placenta praevia; hysterotomy	80	39 F	2	4	1	6·0	18·5	192	22	7	15	2,160 14th day	Discharged 28th day
Placenta praevia and accreta; hysterectomy	91	30 F	4	4	1	8·4	15·5	178	16	12	13	2,460 15th day	Discharged 21st day
Trauma Group													
Multiple injuries	1	25 M	5	4	1	6·0	13·1	342	—	—	—	—	Died 9th day
Cysto-ileoplasty	19	44 M	5	<1	1	5·6	14·8	176	—	Incontinent	—	Approx. 2,000	Died 19th day
Cystectomy; uretero-sigmoidostomy	20	59 M	7	<1	2	7·8	13·5	282	55	<7	—	1,605 14th day	Died 20th day
Hysterectomy; haemorrhage	22	40 F	5	<1	4	5·7	12·2	208	78·5	24	—	780 24th day	Died 26th day
Per-urethral prostatectomy	24	67 M	3	6	2	7·5	8·8	202	32	—	—	300 15th day	Died 17th day
Aortic valvuloplasty	40	58 M	5	2	2	7·6	19·1	204	30	—	—	—	Died 13th day
Wertheim's hysterectomy	41	44 F	5	5	1	3·9	19·1	184	—	>500 on admission	12	3,180 14th day	Discharged 78th day
Secondary haemorrhage; appendicectomy	45	32 M	4	<1	3	7·8	25·1	312	46	—	—	—	Died 10th day
Multiple injuries	46	29 M	5	<1	4	8·6	13·1	256	43	20	27	11,940 53rd day	Discharged 80th day
Aortic graft	49	64 M	3	1	1	7·2	25·1	172	26	9	10	1,760 22nd day	Discharged 28th day
Partial gastrectomy	50	55 M	9	<1	1	6·1	24·2	212	—	—	—	—	Died 12th day
Parathyroidectomy; acute pancreatitis	53	57 F	7	<1	1	3·4	9·6	180	—	—	—	—	Died 8th day
Per-urethral prostatectomy	61	51 M	11	<1	7	6·1	11·3	225	50	32	—	1,200 34th day	Died 36th day
Multiple injuries	69	30 M	11	<1	1	7·4	—	272	>30	Incontinent	17	9,835 22nd day	Discharged 27th day
Partial gastrectomy; incompatible blood transfusion	73	48 F	3	<1	1	4·9	26·4	138	20	9	18	3,800 17th day	Discharged 24th day
Burns	79	24 M	4	2	2	6·7	21·1	236	40	—	—	—	Died 12th day
Acute dehydration; nephrectomy	81	58 F	5	<1	1	7·4	Specimen lost	Specimen lost	—	—	—	—	Died 6th day
Multiple injuries	82	44 M	5	<1	3	6·8	11·3	232	42	19	25	3,660 28th day	Discharged 44th day
Laparotomy; staphyloccal enteritis	85	52 M	4	<1	1	4·7	16·4	206	40	—	—	—	Died 6th day
Others													
Hepato-renal syndrome	14	23 M	8	<1	1	8·2	13·5	208	17·8	—	—	—	Died 9th day
" "	26	57 M	2	<1	1	5·1	13·1	216	34	5	11	3,300 10th day	Died 15th day
Mercury poisoning	29	26 M	5	1	1	7·1	12·2	292	40	9	19	4,900 24th day	Discharged 34th day
Hepato-renal syndrome	37	63 M	8	2	1	4·0	30·2	228	—	11	13	3,960 31st day	Discharged 67th day
Aortogram	44	62 F	8	<1	1	4·5	22·0	242	—	—	—	—	Died 19th day
Diabetic coma	47	13 F	4	<1	1	2·6	7·9	92	17	6	16	4,040 14th day	Discharged 36th day
Pyloric stenosis	48	44 M	3	5	1	4·3	17·5	250	21·5	12	15	2,774 18th day	Discharged 33rd day
Hepato-renal syndrome	51	47 M	8	<1	2	9·0	13·0	222	33	—	—	—	Died 14th day
Aortogram	70	33 M	5	3	1	5·0	16·8	160	22	12	15	3,375 17th day	Discharged 24th day

the 10th day. Thirteen patients had to be dialysed within 24 hours of admission to the kidney unit, and in seven of these a dialysis had to be performed as an emergency on admission. Nine patients required more than one dialysis, and the greatest number performed on one patient was 7 (Case 61).

The blood chemical findings on these patients are important. At the time of the first dialysis only one (Case 73) had a B.U.N. of less than 170 mg./100 ml., whilst in the seven patients who were dialysed as soon as possible after admission six had a B.U.N. greater than 200 mg./100 ml.

In eight patients the potassium level at the time of the first dialysis exceeded 7 mEq/l., and the CO_2 combining power was below 14 mEq/l. in eight patients.

These chemical findings must be considered in conjunction with the clinical state of the patients. In all these patients the clinical deterioration was more rapid than in the other two groups of patients with acute reversible renal failure. In particular we would single out mental deterioration as the most constant finding. Gastric disturbance, such as nausea and vomiting, was also frequent, but an acidotic type of respiration was infrequent, whilst uraemic hypotension was present in only five patients at the start of the first dialysis and bore no specific relationship to the degree of uraemia, except in one patient who had hyperkalaemia.

It was possible to assess the average daily rise in the B.U.N. in 13 of these patients, and in 11 it was 30 mg./100 ml. or over (average rise 46 mg.). This rise, indicating the degree of protein katabolism, was much higher than in the pregnancy group, and accounts in part for the greater number of dialyses that were required for these patients in the traumatic group. The average time taken for the B.U.N. to start falling was 18 days, which was slightly less than in the pregnancy group.

The maximum urinary volume per 24 hours in the patients who recovered varied from 1,760 to 11,940 ml., and appeared to be higher than in the pregnancy group. The patient who passed the largest volume of urine, 11,940 ml. per 24 hours, was given "pitressin," but no reduction of urine volume was noted.

Those patients who recovered had a protracted stay in hospital before discharge, but this was necessary for treatment of their initial lesion rather than their renal function.

Deaths. — Thirteen patients died. In five renal function was recovering, death occurring after the 16th day either from complications of the primary lesion or from sepsis. In the remaining eight patients death occurred earlier than the 14th day before there was evidence of the return of renal function. Only one patient (Case 1) died in uraemia: death occurred in a convulsion during the dialysis. In the remainder the uraemia had been kept under control by dialyses. Eight patients died from sepsis, one from acute pancreatitis, and another, who had had a valvulotomy for an aortic stenosis, developed an acute cardiac arrest during his second dialysis. Two patients died from overhydration, and both had received massive intravenous therapy before they were transferred to our care.

Trauma: Non-dialysed

Six patients in this group were not dialysed (Table V). Five of these died in uraemia before a dialysis could be

TABLE V.—*Findings in Patients who were not Dialysed for Acute Reversible Renal Failure*

Case No.	Cause	Age and Sex	Day Transfer to Kidney Unit	Plasma Levels: Highest K mEq/l.	Plasma Levels: Highest B.U.N. mg./100 ml.	Plasma Levels: Lowest CO_2 c.p. mEq/l.	Average Daily Rise B.U.N. mg./100 ml.	Day Urine Output Exceeded 500 ml./24 Hours	Day 1st Fall in B.U.N.	Maximum Urine Output ml. 24 Hours	Outcome
					Pregnancy Group						
1 N	Accidental haemorrhage	26 F	5	9·0	181	15·5	21	—	—	240	Died 13th day
3 N	,, ,,	29 F	3	6·1	168	15·0	8	8	17	2,900 24th day	Discharged 29th day
4 N	Placenta praevia; caesarean section	24 F	1	4·1	145	15·5	—	3	5	3,810 6th day	Discharged 17th day
5 N	Hypotension; forceps delivery	27 F	7	Not forwarded		—	—	—	—	—	Died 30 min. after admission
11 N	Abortion	21 F	3	4·1	138	23·2	—	Over 500 ml. on admission	4	2,010 13th day	Discharged 16th day
13 N	Post-partum haemorrhage; ? incompatible blood transfusion	26 F	7	4·1	91·5	22·4	—	,, ,,	7	2,490 12th day	Discharged 15th day
14 N	Abortion	26 F	10	6·6	150	16·4	13	11	11	2,788 14th day	Discharged 31st day
15 N	,, ...	21 F	1	4·3	137	15·8	—	2	3	2,480 4th day	Discharged 11th day
					Trauma Group						
6 N	Cholecystectomy ..	75 F	7	Not forwarded		—	—	—	—	—	Died 12 hr. after admission
7 N	Partial gastrectomy ..	69 M	4	8·7*	220	15·0	—	—	—	—	Died 30 min. after admission
9 N	Suture of burst abdomen	52 F	2	4·6	114	20·2	—	3	5	2,330 9th day	Discharged 11th day
12 N	Multiple injuries ..	28 M	6	9·4*	183	—	—	—	—	—	Died 1 hr. after admission
16 N	,, ,, ..	19 M	5	8·1	158	23·4	—	—	—	—	Died 3 hr. after admission
17 N	Haematemesis; partial gastrectomy	49 M	7	5·8*	202	—	—	—	—	—	Died 2 hr. after admission
					Others						
2 N	Haemophilia; blood transfusion reaction	28 M	5	7·5	275	15·5	—	7	10	4,970 15th day	Discharged 21st day
8 N	Ulcerative colitis; blood transfusion reaction	44 F	3	6·4	168	18·0	—	10	13	4,546 17th day	Discharged 30th day
10 N	Intravascular haemolysis	22/12 M	3	5·1	298	12·6	12	Incontinent	11	Incontinent	Discharged 42nd day
18 N	Pneumonia	68 F	5	5·4	211	15·5	24	6	10	1,624 28th day	Discharged 64th day

* This and the other blood chemical findings were sent with the patient.

attempted—four within three hours of admission; the other was admitted when the artificial kidney was in use, and died 12 hours later. (A further patient, not included in this series, died in an ambulance before reaching this hospital.) These cases are recorded to emphasize the importance of referring this traumatic group of patients to an artificial kidney unit early, for all five patients died seven days or less after the onset of renal failure.

The one patient who survived developed an acute renal failure following the suture of a burst abdomen.

Others: Dialysed

Thirteen patients with acute reversible renal failure who were admitted to the unit did not fall into the previous two groups. The renal lesion was precipitated by various factors.

Nine of these patients had to be dialysed and five recovered. The findings are summarized in Table IV. All were admitted eight days or less after the onset of renal failure, and all were dialysed on or before the 10th day. Five required a dialysis within 24 hours of admission. At the time of the first dialysis seven had a B.U.N. in excess of 200 mg./100 ml. Case 47 had diabetes, and although the blood-sugar level had been controlled with insulin she was admitted in uraemic coma with a CO_2 combining power of 7.9 mEq/l. in spite of a B.U.N. of only 92 mg./100 ml. The remaining patient, who had a B.U.N. less than 200 mg./100 ml. (Case 70), was dialysed for uraemic convulsions, which developed quite unexpectedly.

In those patients who survived, the B.U.N. started to fall between the 13th and 19th days—that is, earlier than in the pregnancy and traumatic group. The maximum 24-hour urinary output averaged 3,800 ml., about 1,000 ml. more than the average for the pregnancy group.

Deaths.—Four patients died—two from sepsis (in one of these renal function had recovered), one from a perforated duodenal ulcer, and one was admitted and died in pulmonary oedema from overhydration.

Others: Non-dialysed

The remaining four patients in this group did not require a dialysis, and all recovered. The findings are summarized in Table V. Case 2 N was a haemophiliac, and although the B.U.N. rose to 275 mg./100 ml. and the plasma potassium level reached 7.5 mEq/l., the clinical condition remained good. The B.U.N. in the child (Case 10 N) reached a maximum of 298 mg./100 ml., but the clinical condition was satisfactory. He, however, became drowsy and vomited frequently during the early part of the recovery phase.

Results in Reversible Post-renal Obstruction

The findings in the nine patients who had reversible post-renal obstruction and uraemia are summarized in Table VI.

Seven had prostatic obstruction with retention of urine. The degree of uraemia according to the blood chemical findings was not severe except in one patient (Case 65) who had a B.U.N. of 198 mg./100 ml., and a plasma potassium level of 7 mEq/l., which was lowered by means of cation exchange resins prior to the dialysis. All these patients had severe clinical symptoms, consisting in some of nausea and vomiting and in others of gross mental retardation. After dialysis all were improved clinically; the most striking improvement occurred in their mental state, and all became co-operative and interested in their surroundings. In three of these patients prostatectomy was performed seven days or less after the dialysis, but in the other four prostatectomy had to be delayed until renal function had improved, and in Case 89 two further dialyses were required, the first having been performed as an emergency to control uraemic convulsions.

TABLE VI.—*Findings in Patients who were Dialysed for Reversible Post-renal Obstruction*

Cause	Case No.	Age and Sex	No. of Dialyses	Plasma Levels at 1st Dialysis: K mEq/l.	Plasma Levels at 1st Dialysis: CO_2 c.p. mEq/l.	Plasma Levels at 1st Dialysis: B.U.N. mg./100 ml.	Operation Days after Dialysis	Outcome
Prostatic obstruction	15	69 M	1	6·2	20·8	62	7	Discharged
,,	16	78 M	1	4·75	22·5	59·5	12	,,
Ureteric obstruction	27	37 F	2	4·95	14·8	292	2	,,
Carcinoma bladder	38	60 M	1	6·4	25·1	164	2	Died after cystectomy
Prostatic obstruction	56	63 M	1	3·1	23·2	101	17	Discharged
,,	65	76 M	1	4·0	10·4	198	28	,,
Prostatic obstruction. Chronic nephritis	77	55 M	1	4·4	20·6	65	3	,,
Prostatic obstruction	86	68 M	1	5·1	24·5	104	2	,,
,,	89	34 M	3	4·0	13·1	168	26	,,

The remaining two patients had an obstruction at the ureterovesical junction. One is described below. The second had a carcinoma of the bladder involving both ureteric orifices; a dialysis corrected the uraemic state, and a nephrostomy was successfully carried out, but he died after a total cystectomy.

Infection

Early in this series we encountered a high incidence of infection which caused the death of several patients. The organism chiefly responsible was tetracycline-resistant *Staphylococcus aureus.* This finding led us to examine more closely the bacterial flora of the noses and faeces of those patients admitted with acute reversible renal failure. Of 24 patients so investigated, 15, at the time of their transfer to our unit, were harbouring a tetracycline-resistant strain of staphylococcus, in four a penicillin-sensitive strain was isolated, and in five no staphylococci were found. During the patients' stay in our wards reverse barrier nursing was carried out, and the blankets were subjected to frequent chemical sterilization. In four of the nine patients who were not carrying an antibiotic-resistant staphylococcus on admission, the organism was subsequently isolated during their stay in our hospital. One remained free from this organism, whilst inadequate records were available in four.

The incidence of an erythromycin-resistant strain of staphylococcus was significant. Three patients were admitted harbouring this organism, and it occurred in a further five during their stay in our unit (three of these were treated with erythromycin when staphylococcal enteritis occurred).

Seven patients developed severe staphylococcal enteritis, and were treated with erythromycin at the onset of symptoms and recovered. This was in sharp contrast to those who were not treated at the onset of symptoms but in whom we awaited the result of bacteriological examination of the stools (see Case 22 below). It seems to us that it is dangerous to delay treatment when severe diarrhoea develops in acute renal failure, and at the moment we are guided by the staphylococcal sensitivity patterns obtained from the nose and faeces when routine investigations are made. It should be noted that we have not encountered diarrhoea in these patients except when staphylococcal enterocolitis has developed.

For the past 16 months we have refrained from using any antibiotics prophylactically. We believe that this has reduced the incidence of staphylococcal enteritis, and there has been no increase in other types of infection.

Representative Case Reports

Case 43

A woman aged 35 developed pre-eclampsia, and a concealed accidental haemorrhage precipitated anuria. Delivery of a stillborn child was associated with periods of hypotension (80/50), treated with blood transfusions. Two days later slight jaundice was present. The dietary regime was instituted on the second day of anuria, and she was transferred to Leeds on the seventh day. At this time there was moderate oedema with vomiting, but her mental state appeared normal. Blood chemistry showed severe uraemia, and the first dialysis was performed on the eighth day, with a good chemical and clinical response (Fig. 2). On the 11th day she suddenly became mentally deranged and refused all treatment. The second dialysis was performed on the 12th day with the aid of light anaesthesia, and the mental state returned to normal within 24 hours. A further transient mental derangement occurred on the 19th day, but renal function was now returning. During the oliguric phase there was moderate diarrhoea and a tetracycline - resistant staphylococcus was isolated from the faeces, but the condition cleared spontaneously.

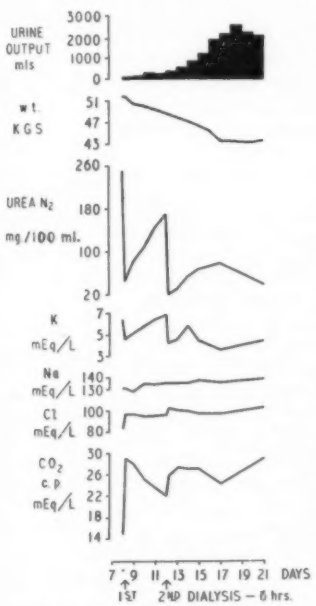

FIG. 2.—Case 43. Chemical findings in a patient who developed acute reversible renal failure following an accidental haemorrhage.

Case 18

A woman aged 31 had an evacuation of the uterus for an inevitable abortion. At the time the uterus was irrigated profound shock occurred; the B.P. fell to 70/55, and this was restored with 1 pint (570 ml.) of dextran and 1 pint of blood. Anuria was present after the operation. Jaundice occurred 24 hours later. She was not treated by a strict dietary regime, and six days later was transferred to Leeds. The following day she began to vomit, and the first dialysis was performed on the eighth day of anuria (Fig. 3), the CO_2 c.p. being 10.5 mEq/l., and the B.U.N. 118 mg./100 ml. The dialysis had to be terminated after four and a half hours, as a technical fault developed in the machine. After the dialysis she took glucose, water, and vitamins orally, but by the 16th day the clinical condition had deteriorated, the CO_2 c.p. had fallen to 11.3 mEq/l., and a second dialysis, lasting six hours, was carried out. Another good clinical response was obtained. The urine volume started to increase

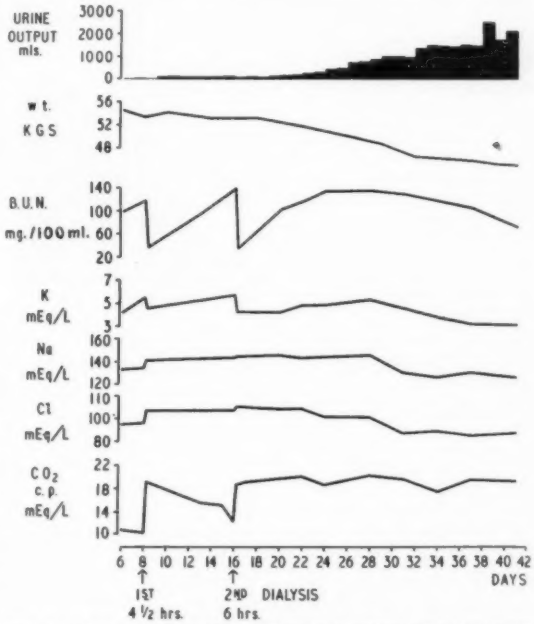

FIG. 3.—Case 18. Chemical findings in a patient who developed acute reversible renal failure following an abortion.

after the 24th day, and the B.U.N. began to fall on the 31st day. On the 30th day nausea returned, and as she was unable to take the requisite quantity of fluid orally some was given subcutaneously.

On the 35th day she started to vomit more copiously, and in order to administer food it was necessary to give milk by intragastric drip and suppress the vomiting with chlorpromazine. Three days later the vomiting ceased and she then made an uninterrupted recovery. The maximum urine output during the recovery phase was 2,930 ml.

After the second dialysis diarrhoea occurred and a tetracycline-resistant staphylococcus was isolated from the faeces. The diarrhoea cleared spontaneously.

Case 46

In a motor-cycle accident a man aged 29 received a fracture-dislocation of the right hip with injury to the sciatic nerve, multiple fractures of the pelvis, a fractured vault of skull, and concussion. The B.P. was reported as unrecordable for six hours after injury, and he was given 6 pints (3.4 litres) of blood. Anuria was present from the time of injury and the dietary regime was instituted on the third day. He was transferred to Leeds on the fifth day because of rapid clinical deterioration. The recent head injury accounted for a semi-stuporous state. He was of excellent physique. Slight jaundice was present. The blood chemical findings showed severe uraemia (Fig. 4), and the first dialysis was necessary immediately. Ion-exchange resins were used subsequently to control the plasma level of potassium, which was rising disproportionately. Because of the head injury, the mental state was unreliable as a guide for clinical assessment of uraemia. A B.U.N. level in excess of 200 mg./100 ml. was used as the main guide for further dialyses,

and these were necessary on the 10th, 14th, and 18th days. Urine output started to increase on the 20th day, but a fall in the B.U.N. did not occur until the 27th day. A full diet was started at this time. Urine output rose to approximately 12 l. a day, which was unaffected by administration of pitressin, but it subsequently fell to 5–6 l. a day.

His mental state returned to normal about the 36th day. His katabolism was very high, and during the period of renal failure his subcutaneous fat and his musculature wasted dramatically. During the recovery phase his appetite

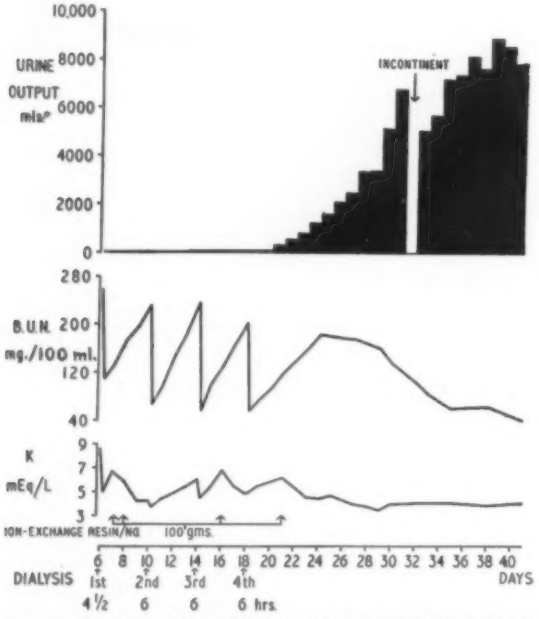

FIG. 4.—Case 46. Chemical findings in a patient who developed acute reversible renal failure following multiple injuries.

became voracious, and he had apparently replaced most of his lost tissues by 14 weeks after injury. He subsequently responded well to orthopaedic treatment of his residual disabilities.

Case 22

A woman aged 40 developed a severe intra-abdominal haemorrhage 24 hours after a hysterectomy for fibroids. A laparotomy was performed, but further haemorrhage resulted in periods of hypotension. Anuria developed at the time of the first haemorrhage, and the dietary regime was instituted from the second day. On the fifth day ureteric catheterization showed that there was no urinary obstruction, and she was transferred to Leeds the same day.

On admission she was drowsy, responding only to simple questions. There was acidotic breathing, pitting oedema of the sacrum and lower limbs, basal crepitations, and slight jaundice. Blood chemical findings included a B.U.N. of 208 mg./100 ml., and a CO_2 c.p. of 12.2 mEq/l. (Fig. 5). Dialyses were necessary immediately on admission and again on the 8th and 13th days. Oxytetracycline, 400 mg., was given prophylactically after each dialysis. After the third dialysis her clinical condition improved considerably, but on the 18th day severe diarrhoea developed and general clinical deterioration with circulatory failure followed. A fourth dialysis was performed on the 19th day, and, after bacteriological reports had shown the faeces to contain a tetracycline-resistant staphylococcus, erythromycin was begun on the 22nd day. Clinical deterioration continued, and the patient died on the 26th day, although by this time the urinary output had reached 718 ml. a day.

Necropsy showed the mucosa of the proximal three-quarters of the large intestine to be studded with

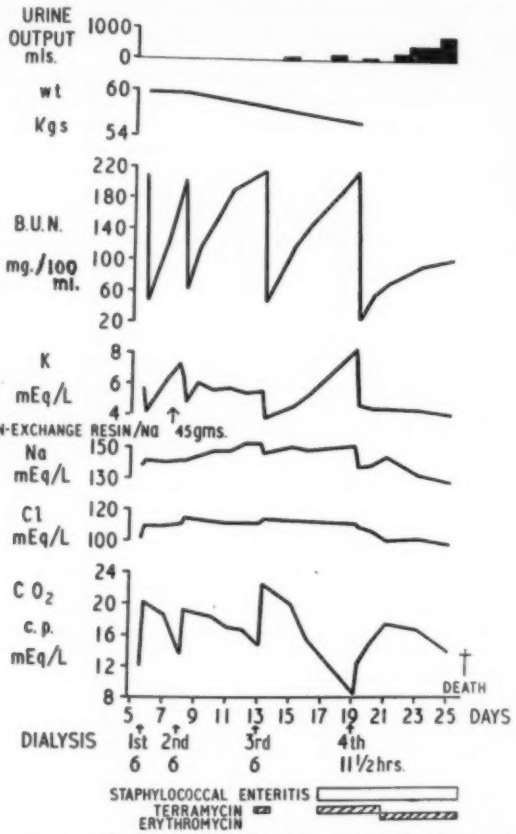

FIG. 5.—Case 22. Chemical findings in a patient who developed acute reversible renal failure following an intra-abdominal haemorrhage.

innumerable ulcers. In the lungs there were minute pyaemic abscesses, and the brain contained a single abscess about ¼ in. (2 cm.) in diameter. *Staph. aureus* was cultured from these affected areas. Histological examination of the kidneys showed a recovering tubular necrosis.

Case 27

A woman aged 37 had a left tuberculous pyonephrosis with an impassable stricture of the left ureter 3 cm. from the ureteric orifice. There was a right ureterocele (which had been treated by diathermy) and a right hydronephrosis and hydroureter. The uraemia was treated by dialysis. Later she developed severe hypertensive attacks while being treated in the sanatorium, and it was decided to remove the left kidney and ureter in the hope that the hypertension would decrease and that the function of the right kidney might improve. As the blood chemical findings suggested that a severe degree of uraemia might ensue after the operation, a pre-operative

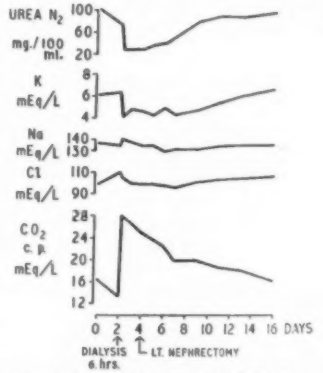

FIG. 6.—Case 27. Chemical findings in a patient who had a pre-operative dialysis for chronic renal disease.

dialysis was performed (Fig. 6) and the uraemic state was corrected. The clinical condition of the patient improved also. 48 hours later a left nephro-ureterectomy was performed. The post-operative period was entirely uneventful even though the blood chemical levels gradually returned to the levels existing prior to the dialysis. Sodium and chloride supplementation was required in the immediate post-operative period as she had a salt-losing nephritis.

After the nephrectomy the hypertension disappeared though no further improvement in the function of the right kidney was noted. Two months after her discharge we were informed that she had developed a right pyelonephritis, and had died.

Discussion

Although haemodialysis is a safe procedure it has a restricted use in the treatment of patients with renal failure. We have found it of most value in the treatment of acute reversible renal lesions, and reversible post-renal obstruction presenting with uraemia.

Indications for Performing a Dialysis

The main purpose of dialysis is to decrease the mortality in patients with the reversible types of renal failure and to make the clinical management easier. In keeping with these principles we have accepted as indications for dialysis, firstly, clinical changes which may presage deterioration, and, secondly, those changes in the blood chemistry that are generally accepted as constituting a hazard to life. We have found that the clinical changes are more important than the chemical ones.

In the first category we have placed early mental changes, such as mental retardation or developing uncooperation, and persistent nausea and vomiting. We advocate dialysing before the onset of convulsions, semicoma, severe mental confusion, or uraemic hypotension. In our series the earliest mental change has been regarded as serious, and if deterioration progresses then a dialysis must be performed as soon as possible, if necessary throughout the night.

In the second category we advocate dialysis if the CO_2 combining power falls below 13 mEq/l. or the plasma potassium level exceeds 7 mEq/l. The use of ion-exchange resins should be reserved for those instances where the potassium level is rising out of proportion to the other indices of uraemia.

The level of the blood urea is important, not because urea has any toxic properties, but because the level acts as an indicator of the breakdown of protein. We have been impressed from the beginning by the regularity of one or more of the clinical indications for dialyses arising at about the same time that the B.U.N. reaches 180–200 mg./100 ml. (blood urea 385–428 mg./100 ml.). We have witnessed relatively sudden deterioration and death in these circumstances, and, having satisfied ourselves that a dialysis is a safe procedure and that nothing is to be gained by waiting until the last possible moment, we have now added a B.U.N. of 180–200 mg./100 ml. as an indication for dialysis. It is emphasized that these three chemical indications need not be present at the same time, and we consider each as an indication in its own right.

These indications should still be applied whether the patient is anuric or entering the recovery phase. Even if the urine output is increasing but the clinical and chemical assessments show that the uraemia is becoming more pronounced, it is far safer to dialyse. Whether or not the patient would have survived without a dialysis in such circumstances is quite academic, for the rapid improvement that occurs makes the ultimate recovery more certain.

Special mention is required for those patients presenting with a post-renal obstruction causing uraemia, for the renal function usually recovers sufficiently to allow the patients to live a useful life, once the uraemia has been relieved by surgical procedures. The clinical condition of these patients has often deteriorated more than the examination of the blood chemistry would suggest, and the decision to dialyse has been made more on clinical assessment. When the obstruction occurs in the upper renal tract dialysis should be followed within 48 hours by surgical relief of the obstruction. When the prostate gland causes obstruction it is safer to treat the patient initially with an indwelling catheter and correct the uraemia by dialysis. Operation should be delayed until renal function has partially recovered, a further dialysis being performed immediately before operation when indicated. Particular attention must be given to the care of the patient with an indwelling catheter so that ascending infection is prevented (Pyrah, Goldie, Parsons, and Raper, 1955; Gibbon, 1958). This is vital, as prolonged catheter drainage may be required before the patient is fit to withstand a prostatectomy.

Metabolic Response

Some workers have been impressed by the variation in mortality of patients with acute renal failure according to the primary disease (Teschan, Post, Smith, Abernathy, Davis, Gray, Howard, Johnson, Klopp, Mundy, O'Meara, and Rush, 1955; Taylor, 1957). It is generally agreed that those cases complicating trauma (such as war injuries, road accidents, or major surgical procedures) have a less favourable prognosis than cases in which renal failure is the main feature (such as transfusion reactions or hypotension complicating an abortion). Other workers, dealing mainly with non-traumatic cases, have emphasized the good results that can be obtained with a dietary regime alone when the period of oliguria has been less than say 10–14 days (Bull, Joekes, and Lowe, 1949).

In assessing our cases we have been impressed by an association between the severity of the illness and the metabolic response of the patient as measured by the speed at which uraemia develops, for which the daily rise of the B.U.N. is the best available laboratory index. The urea production which occurs in normal persons, or in patients with uncomplicated renal failure, whilst taking the dietary regime would correspond to a daily rise of the B.U.N. of less than 10 mg./100 ml. a day if anuria was present (Gamble, 1947; Parsons and McCracken, 1957). We have, wherever possible, classified our cases as mild, moderate, or severe acccording to the rate of rise of the B.U.N. a day whilst anuric and receiving the standard dietary regime.

The mild group (Table VII), where the rise is less than 15 mg./100 ml. a day, can for the most part be managed without the need for dialysis, and perhaps the majority of patients in this category have been managed successfully in their own hospitals. The two patients who were dialysed had either inadequate treatment or an unduly protracted oliguric phase. Those patients that came into the moderate group (B.U.N. rise 15–30 mg./100 ml. a day) and the severe group (B.U.N. rise greater

than 30 mg./100 ml. a day) had evident causes of an increased metabolic breakdown. A study of our cases shows that the majority of anurias associated with the complications of late pregnancy have fallen into the moderate group (Parsons and McCracken, 1958b), whilst the majority of cases following major surgery or trauma have fallen into the severe group (11 out of the 15 patients, Table VII). Whilst the primary condition

TABLE VII.—*Average Rise of B.U.N. in Patients With Acute Reversible Renal Failure*

Group	Average Daily Rise B.U.N. mg./100 ml.	No. of Patients	No. Dialysed	No. Recovered
Mild	<15	5	2	5
Moderate ..	15–30	20	18	18
Severe	>30	15	15	5

which precipitated the acute renal failure seems largely to determine the degree of metabolic response, complications can increase the response. For instance, one patient initially fell into the mild group, but the occurrence of a staphylococcal enteritis rapidly increased the metabolic response, so that the B.U.N. rose at a greater rate than 30 mg./100 ml. a day.

The importance of assessing the severity of the metabolic breakdown is stressed for several reasons. (1) The moderate and severe groups will probably require dialysis for survival. (2) Cases in the severe group will require dialysis so soon after diagnosis that no time must be lost in transferring them to an artificial kidney unit. (3) Cases in the severe group have a high mortality, and all the complications in addition to the uraemia must be treated adequately. (4) It affords some basis for comparison of results in different series.

Reduction of the Metabolic Response by Hormones.—Although testosterone has been used to reduce the metabolic response in patients with acute renal failure the evidence is not conclusive (Merrill, 1955). We have described elsewhere (McCracken and Parsons, 1958) that the synthetic anabolic steroid norethandrolone ("nilevar"; 17-ethyl-19-nortestosterone) reduces protein katabolism by approximately 70% in patients who have developed acute renal failure as a complication of pregnancy. Norethandrolone has been used in other conditions, but no significant reduction of protein katabolism was observed. We would now advocate giving norethandrolone (30 mg. a day) to all patients with acute reversible renal failure occurring as a complication of pregnancy, as it might largely eliminate the need for dialysis (Parsons, 1959).

Recovery Phase of Acute Reversible Renal Failure

The period of oliguria has usually been expressed in terms of urine volume per 24 hours. This has little practical value. For instance, in mild cases we have observed correction of the uraemic state when the urine volume has been as low as 700 ml. a day, whilst in the severe case uraemia may be increasing when the urine output is 1,200 ml. a day. The correction of the uraemic state in these patients is dependent on the rate of katabolism of protein as well as the degree of renal function. It should be remembered that the patient will continue to deteriorate until the B.U.N. starts to fall as a result of returning renal function. This event is more important than the return of urine volume to any particular figure.

We have found that the maximum daily volume of urine during the late recovery phase is usually about 3–4 l., except when overhydration has occurred, and then it is correspondingly higher. We would agree with Merrill (1955) that ionic supplementation is usually unnecessary in this phase when the patient is eating a normal diet.

Optimum Time for Transfer

Many of the patients with acute renal failure have been referred to us with advanced clinical deterioration due to uraemia. This has occurred most frequently in the traumatic group, where the high metabolic rate produces uraemic manifestations early in the course of the illness. Of the 19 patients in the traumatic group, 13 required dialysis seven days or less after the onset of anuria, and nine of these on or before the fifth day. Many of these patients had to be dialysed as an emergency on admission, for, according to our criteria, they had been allowed to progress too far before transfer. It is therefore imperative that these patients should be transferred earlier, and if possible 48 hours before the optimum time for dialysis, for if this has passed the chances of survival are lessened. Daily observations of the rise of the blood urea give a reliable index of the rate of progress towards the uraemic state, and will forecast the day the B.U.N. reaches 180–200 mg./100 ml.

Patients in the moderate group usually require a dialysis between the 6th and 10th days after the onset of anuria, and again transfer should be arranged early.

When a patient develops an acute reversible renal failure we advocate that the nearest artificial kidney unit should be informed so that when the need for transfer becomes apparent it can be arranged early. This should save the distressing sight of seeing some patients die within a few minutes or hours of admission, and should save the artificial kidney team from having to use the machine throughout the night.

Infection

Uraemic patients are very susceptible to infection and, in particular, to staphylococcal enterocolitis. It should be noted that we have not encountered diarrhoea in these patients except when staphylococcal enterocolitis has developed. Bull (1955) advocated the routine administration of penicillin to patients with acute renal failure, but to-day the high incidence of antibiotic-resistant strains of staphylococci demands a reassessment. Our experience suggests that it is unwise to administer broad-spectrum antibiotics prophylactically, as these have undoubtedly precipitated staphylococcal infections in some of our patients. We have tried to minimize infections by reverse barrier nursing and by frequent sterilization of blankets, and have used antibiotics only to treat known infections. The situation, however, must not be viewed with complacency, because staphylococci resistant to erythromycin are now being encountered.

It is important to emphasize that these infections are not due to or associated with the artificial kidney. They occur with the same incidence in patients not treated by dialysis. In some patients infections arose before the dialysis, and it has occurred in uraemic patients who have never received antibiotics. Because these infections

were regarded as terminal events they have not hitherto had the same importance attached to them, but they are of the utmost importance now that the uraemia can be controlled by dialysis.

Demand for Artificial Kidneys

The number of patients who require dialysis are relatively few. For optimum efficiency we would agree with Merrill (1955) that an artificial kidney must be in fairly constant use so that the unit can be maintained at optimum efficiency. It would seem unrealistic, therefore, to have too many of these machines in the country. This is important, for the cost of staffing and maintaining an artificial kidney is considerable. In support of this, we have found that these patients can be transported over long distances (many have travelled over 200 miles—320 km.) with safety, provided that the transfer is arranged early.

There are many types of artificial kidney available. Some of these machines can also remove water from the patient by ultrafiltration (Alwall, Skeggs–Leonards, and Kolff disposable pack), but unfortunately their dialysing surface area, and hence efficiency, is less than the modified Kolff–Brigham model used in this series. Among patients with acute reversible renal failure we have had 15 with a severe metabolic response but only three in whom overhydration was a problem. We regard maximum efficiency of dialysis as more important than the ability to remove water, and therefore prefer the modified Kolff–Brigham machine, as the uraemia can be more effectively treated and controlled.

Summary

A total of 100 patients referred to the artificial kidney unit are reviewed. Of these, 82 were dialysed with an improved Kolff–Brigham artificial kidney. Complications occurring during the dialysis were few and not serious.

Acute reversible renal failure occurred in 63 patients, and 45 were dialysed. The basic treatment was a dietary regime (400 ml. of water and 100 g. of glucose daily, with vitamins). The most consistent indication for dialysis was clinical deterioration, particularly early mental changes, nausea, and vomiting. The biochemical indications were a B.U.N. 180–200 mg./100 ml., K 7 mEq/l., and CO_2 c.p. 13 mEq/l. The metabolic response, estimated by the daily rise of the B.U.N., was remarkably constant in any one patient, and a classification into mild (rise <15/mg./100 ml. a day), moderate (rise 15–30 mg./100 ml. a day), and severe (rise >30 mg./100 ml. a day) is suggested. The mild group were frequently managed successfully without dialysis, whilst the moderate group (mainly complications of late pregnancy) usually required a dialysis between the 6th and 10th days. The severe group (mainly trauma, accidental or surgical) often required a dialysis as early as the fourth or fifth day. In the severe group the incidence of complications, particularly sepsis, was high and the mortality greater. Many of these patients were referred too late; earlier transfer might improve the prognosis.

The metabolic response in the pregnancy patients was reduced by 70% when 30 mg. of norethandrolone ("nilevar") was given daily. Administration of this steroid might largely eliminate the need for dialysis. A similar action has not been observed in other conditions.

Nine uraemic patients with reversible post-renal obstruction have been dialysed. Obstructions in the upper renal tract have been relieved surgically following a dialysis. Obstructions caused by the prostate gland were relieved by an indwelling catheter, and a dialysis was performed, operation being delayed until renal function improved.

In chronic renal failure too few patients have been treated for justifiable conclusions to be drawn. In those patients with acute renal failure of obscure origin dialysis has been used so as to maintain life while diagnostic procedures were being undertaken. If an irreversible condition was found no further dialyses were performed.

The artificial kidney was bought and is being maintained by the Board of Governors of the United Leeds Hospitals. They also defrayed part of the expenses of this investigation. We thank all the consultants who referred patients to the unit. We are grateful to Professor L. N. Pyrah, Mr. F. P. Raper, and Professor R. E. Tunbridge for advice and for help with some of the diagnostic procedures. During the past six months Drs. O. Ciniewicz and C. R. Blagg have given much help in the routine management of the patients. We thank Sisters M. Thwaites, M. Sharpe, and F. N. Ellis, who nursed these patients; Dr. C. K. Anderson for the pathological findings; the staff of the department of bacteriology for the bacteriological findings; Mr. J. Hainsworth for the figures; and Mrs. S. M. Hobson, Miss M. Nicholson, and Mrs. J. McNeill for the biochemical data.

References

Alwall, N. (1947). *Acta med. scand.*, **128**, 317.
Anthonisen, P., Brun, C., Crone, C., Lassen, N. A., Munck, O., and Thomsen, Aa. C. (1956). *Lancet*, **2**, 1277.
Bull, G. M. (1955). Ibid., **1**, 777.
—— Joekes, A. M., and Lowe, K. G. (1949). Ibid., **2**, 229.
—— —— —— (1958). Ibid., **1**, 134.
Danzig, L. E. (1955). *New Engl. J. Med.*, **252**, 49.
Doolan, P. D., Walsh, W. P., Kyle, L. H., and Wishinsky, H. (1951). *J. Amer. med. Ass.*, **146**, 105.
Gamble, J. L. (1947). *Harvey Lect.*, **42**, 247.
Gibbon, N. (1958). *Brit. J. Urol.*, **30**, 1.
Hamburger, J., and Richet, G. (1956). *Rev. franç. Ét. clin. biol.*, **1**, 39.
Kolff, W. J. (1957). *Circulation*, **15**, 285.
—— and Berk, H. Th. J. (1944). *Acta med. scand.*, **117**, 121.
Kyle, L. H., Jeghers, H., Walsh, W. P., Doolan, P. D., Wishinsky, H., and Pallotta, A. (1953). *J. clin. Invest.*, **32**, 364.
Legrain, M. (1953). *Sem. Hôp. Paris*, **29**, 353.
McCracken, B. H., and Parsons, F. M. (1958). *Lancet*, **2**, 885.
Merrill, J. P. (1950). *Ann. intern. Med.*, **33**, 100.
—— (1955). *The Treatment of Renal Failure*. Grune and Stratton, New York and London.
—— Thorn, G. W., Walter, C. W., Callahan, E. J., and Smith, L. H., jun. (1950). *J. clin. Invest.*, **29**, 412.
—— and Weller, J. M. (1952). *Ann. intern. Med.*, **37**, 186.
Moore, F. D., and Ball, M. R. (1952). *The Metabolic Response to Surgery*. Thomas, Springfield.
Murphy, W. P., jun., Swan, R. C., jun., Walter, C. W., Weller, J. M., and Merrill, J. P. (1952). *J. Lab. clin. Med.*, **40**, 436.
Parsons, F. M. (1954). *Brit. J. Urol.*, **26**, 7.
—— (1959). *Lancet*, **1**, 148.
—— and McCracken, B. H. (1957). *Brit. J. Urol.*, **29**, 424.
—— —— (1958a). Ibid., **30**, 463.
—— —— (1958b). *J. Obstet. Gynaec. Brit. Emp.*, **65**, 631.
Pyrah, L. N., Goldie, W., Parsons, F. M., and Raper, F. P. (1955). *Lancet*, **2**, 314.
Ramwell, P., Parsons, F. M., and McCracken, B. H. (1959). To be published.
Shackman, R., and Milne, M. D. (1957). *Brit. J. Urol.*, **29**, 434.
Skeggs, L. T., jun., and Leonards, J. R. (1948). *Science*, **108**, 212.
Sorrentino, M. (1956). *La Depurazione Extra-renale*, Abruzzini Ed., Rome.
Teschan, P. E., Post, R. S., Smith, L. H., jun., Abernathy, R. S., Davis, J. H., Gray, D. M., Howard, J. M., Johnson, K. E., Klopp, E., Mundy, R. L., O'Meara, M. P., and Rush, B. F., jun. (1955). *Amer. J. Med.*, **18**, 172.
Taylor, W. H. (1957). *Lancet*, **2**, 703.
Thaysen, J. H., Gjørup, S., and Killimann, S. (1957). *Dan. med. Bull.*, **4**, 73.
Weller, J. M., Swan, R. C., and Merrill, J. P. (1953). *J. clin. Invest.*, **32**, 729.

STREPTOMYCIN POISONING IN RENAL FAILURE

AN INDICATION FOR TREATMENT WITH AN ARTIFICIAL KIDNEY

BY

K. D. G. EDWARDS*, M.B., B.S.

AND

H. M. WHYTE, D.Phil., M.B., M.R.C.P., M.R.A.C.P.

From the Clinical Research Department, Kanematsu Institute, Sydney Hospital, Sydney, Australia

It is well known that streptomycin can cause vestibular damage resulting in attacks of vertigo and loss of balance and that deafness sometimes occurs concurrently. Loss of vestibular function is usually permanent and may be completely disabling, although some patients, especially the younger ones, learn to use compensatory mechanisms and so reduce their symptoms (Cawthorne and Ranger, 1957).

There is considerable variation in the amounts of streptomycin reported to have caused toxic effects, but, being normally excreted in the urine, overloading and toxicity are much more likely to occur when renal function is defective. The first five cases we report here emphasize this. But the fact that the drug is normally eliminated from the body by glomerular filtration raises the possibility of removing it in an emergency by extra-corporeal haemodialysis. Tests carried out *in vitro* prove this to be effective, and we now regard streptomycin administration in an oliguric patient as a clear indication for early treatment with an artificial kidney. Freedom from the signs of streptomycin toxicity in five patients treated in this way suggests that the treatment might have some virtue.

Patients with Permanent Vestibular Damage

Five patients have been seen in the past two years with permanent vestibular damage due to streptomycin. All had evidence of renal disease.

Case 1.—A man aged 68 had been found to have a very high blood pressure one year previously. He had no symptoms for three months, then developed a severe infection of the renal tract. He was admitted to hospital, and treated with penicillin, sulphonamides, and 14 g. of streptomycin in one week. He noticed vertigo from the first time he sat on the edge of the bed, and when he was allowed to walk he was noticeably unsteady on his feet. Treatment with pentolinium and rauwolfia for hypertension aggravated the vertigo. The vertigo occurred with any sudden head movement and was often accompanied by migrainous headache. When admitted to Sydney Hospital for investigation he was found to have a blood pressure of 240/160 mm. Hg, he was slightly deaf, and he walked with great difficulty with a wide-based staggering gait. He spent most of the day in bed to minimize vertigo. Special tests showed bilateral perception deafness and absence of vestibular response to caloric stimulation. He had chronic renal failure, with a blood urea level of 110 mg./100 ml., and a specific gravity range of 1018 to 1001.

Case 2.—A woman aged 56 had been hypertensive for 16 years. For the last two years she had been treated for recurrent pyelonephritis with antibiotics, including one course of streptomycin. Ganglion blockade was begun in an attempt to relieve severe headache and breathlessness, but she had some hypotensive attacks, one of which was severe and led to acute oliguric renal failure. She passed very little urine for seven days, during which time she was treated again with a course of streptomycin. When transferred to Sydney Hospital the blood urea level was 300 mg./100 ml. and diuresis began the same day. Convalescence was complicated by marked vertigo on moving her head, sometimes followed by nausea and vomiting. Caloric tests of vestibular function showed no response, although hearing was normal. This loss of balance sense threatened to keep the patient bedridden, but after several weeks she managed to walk slowly if she kept her head steady. When discharged home she was able to walk satisfactorily in this way, although she still became giddy if she moved her head suddenly, and she could not walk in the dark. Her renal function on discharge was severely impaired, with proteinuria and microscopic haematuria present, a blood urea level of 80 mg./100 ml., and a glomerular filtration rate of 17 ml./minute (15% of normal).

Case 3.—A woman aged 56 was admitted to hospital with severe colicky pain in the right loin, vomiting, dehydration, shock, fever, and oliguria. Laparotomy revealed no abnormality. She had injections of penicillin and streptomycin, and noradrenaline was given for 48 hours to maintain the systolic blood pressure above 100 mm. Hg. Urinalysis revealed proteinuria, haematuria, and pyuria. After four days the level of urea in the blood was 90 mg./100 ml., and she appeared to be improving but complained of buzzing noises in her ears. Streptomycin was suspended after 4 g. had been given. She became increasingly deaf in addition to the tinnitus and experienced vertigo whenever she moved her head. This was shown to be due to loss of vestibular function. Subsequent urological investigation showed urethral stenosis, chronic papular cystitis, and small, irregularly contracted kidneys with impaired function. Her acute illness was now thought to have been due to an exacerbation of chronic pyelonephritis. She was discharged home, but was disabled by loss of hearing, giddiness, and ataxia. Her final tests showed a level of urea in the blood of 44 mg./100 ml., and a urea clearance 44% of the standard normal.

Case 4.—A man aged 51 developed acute oliguric renal failure after transfusion of 100 ml. of mismatched blood during an orthopaedic operation. Diabetes mellitus had been discovered two months earlier and was controlled by diet. During the oliguric phase he received penicillin and 6 g. of streptomycin as routine post-operative prophylaxis before being transferred to this hospital. Haemodialysis in the artificial kidney was performed for 10 hours after 10 days of oliguria because of increasing distress from uraemia. Diuresis began and his renal failure was gradually corrected. Four weeks after the first streptomycin injections he noticed vertigo on moving his head, eyes, or arms, and difficulty in balancing. He preferred to be back in bed with his head quite still on the pillows. Caloric tests for vestibular function showed complete bilateral loss. With physiotherapy he gained sufficient confidence to learn to walk again, but he had complete loss of balance sense in the dark, and would fall over if he shut his eyes or suddenly turned his head or eyes. He was quite unable to return to work. When seen eight months later he was depressed and emotionally labile, with no further improvement.

Case 5.—A man aged 28 developed acute oliguric renal failure after a thoracotomy following a penetrating wound of the chest. Routine post-operative injections of penicillin and streptomycin were given, with a total dose of 4 g. of the latter. He was transferred to the clinical research unit, Sydney Hospital, after two weeks of conservative treatment. Haemodialysis was performed for 10 hours the next day because of severe uraemia, acidosis, and overhydration. The subsequent diuresis was uneventful from the biochemical aspect. Four weeks after the first injection of streptomycin he noticed vertigo on moving his head, and found difficulty in walking. He was anaemic, but a subsequent blood transfusion did not improve his symptoms. Caloric tests of vestibular function showed no response. Physiotherapy

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was effective in rehabilitation, and he was able to walk confidently with his head held steady, though he still experienced vertigo with sudden head movements and could not stand with his eyes closed. He continued to improve and was discharged home. Ten months later he still found difficulty in balancing, and caloric tests were still negative. While trout fishing on one occasion he had to travel two miles back to camp over rough country after dark. Walking was impossible because he kept losing his balance, so he crawled the whole way. He now makes sure of returning to camp before nightfall.

Dialysis of Streptomycin in Vitro

A simple, semi-quantitative test showed that streptomycin could be dialysed from blood across the same cellulose membrane as used in the artificial kidney. A small length of "visking" cellulose tubing containing 20 ml. of heparinized blood and 250 mg. of streptomycin was agitated for 18 hours in 500 ml. of 0.85% saline solution. Great care was taken with sterility. The streptomycin content of the bath fluid was measured by a modification of the method described by Mackie and McCartney (1953) in which serial dilutions of the test solution and of standard solutions of streptomycin were tested for their ability to inhibit the growth of the Oxford staphylococcus.

The results showed conclusively that streptomycin crossed the membrane to appear in the dialysing solution. By the end of 18 hours something between 100 and 250 mg. of streptomycin (40–100% of the orginal load) had been transferred from the blood to the bath fluid.

Patients Treated with Early Haemodialysis

Following these experiences it was decided to treat immediately by haemodialysis any further oliguric patients who had had a total dose of more than 1 g. of streptomycin.

Case 6.—A woman aged 30 developed acute renal failure following a severe ante-partum haemorrhage which necessitated a caesarean section and a blood transfusion. Streptomycin was begun two days later, but was stopped after 1.5 g. had been given because she still had oliguria. She was transferred to Sydney Hospital on the eleventh day. Giddiness had appeared and was suggestive of vestibular damage. She had no nystagmus, but complained of vertigo unless she kept her head and eyes perfectly still. She was dialysed as soon as possible for 10 hours. Diuresis began the day after dialysis, and her recovery was uneventful. After five weeks the vestibular responses to caloric stimulation were normal, and she was discharged. Four months later she felt quite well and balance was normal.

Case 7.—A woman aged 38 had acute renal failure caused by a septic abortion due to *Clostridium welchii*. After three days at home she was admitted to hospital, where treatment included an eight-day course of 10 g. of streptomycin. Following this she was transferred to Syndey Hospital. Dialysis was begun as soon as possible, and was continued for four hours; for technical reasons it was stopped earlier than usual. During the oliguric phase, which lasted 18 days, the average urinary output was 400 ml./day. Diuresis followed, and the patient recovered. She had no loss of balance when discharged after nine weeks in hospital. After some weeks at home she noticed giddiness if she moved her head suddenly. She fell twice while out shopping, and had some difficulty in walking, but attributed this to very painful heels. The giddiness passed off, and when seen after four months her balance was normal, and tests of hearing and vestibular function were normal.

Cases 8, 9, and 10.—These patients received injections of 3 to 6 g. of streptomycin during the oliguric phase of acute renal failure. The causes of the renal failure and other details are shown in the accompanying Table, but all resembled Cases 6 and 7 in that they were treated by dialysis and all have remained free of symptoms and signs of streptomycin poisoning.

Discussion

The toxic effects of streptomycin became all too well known in the early days of its use. Smaller doses have since been advocated and the danger of renal insufficiency is better appreciated. The drug is normally eliminated in the urine by glomerular filtration, most of an injected dose being excreted unchanged within 12 hours. However, in severe renal failure very little is excreted and the concentration of streptomycin in the

Patients Given Excessive Doses of Streptomycin

Case No.	Age in Years	Sex	Diagnosis	Streptomycin: Days	Streptomycin: Total Dose (g.)	Streptomycin: Indication	Streptomycin: Daily Urine Volume (ml.)	Streptomycin: Maximum Plasma Urea (mg./100 ml.)	Dialysis Day (Days after Beginning Streptomycin)	Return of Urine Flow Exceeding 1,000 ml. Daily (Days)	Signs of Toxicity
Patients in whom the danger of streptomycin toxicity was not recognized: permanent damage sustained											
1	68	M	Chronic renal failure and hypertension	7	14	Pyelonephritis	Not known	110	—	—	Bilateral loss of vestibular function and impaired hearing
2	56	F	Acute renal failure due to hypotensive therapy; chronic renal insufficiency	6	6?	,,	30	300	—	7	Bilateral loss of vestibular function
3	56	F	Acute exacerbation of chronic renal failure	4	4	,,	400	90	—	5	Bilateral loss of vestibular function and impaired hearing
4	51	M	Acute renal failure; mismatched blood transfusion; laminectomy	3	6	Post-operative prophylaxis	100	320	10	12	Bilateral loss of vestibular function
5	28	M	Acute renal failure after thoracotomy	4	4	,,	30	470	15	16	,, ,,
Patients treated with dialysis specifically to remove streptomycin: no permanent damage detected											
6	30	F	Acute renal failure; ante-partum haemorrhage and caesarean section	1	1·5	Prophylaxis	240	355	9	10	Vertigo after 8 days, lasting for 2 days. Caloric tests normal
7	38	F	Acute renal failure; septic miscarriage	8	10	Septicaemia due to *Cl. welchii*	400	525	9	15	Giddiness after 80 days, lasting for some weeks. Caloric tests normal
8	38	F	,, ,, ,,	5	5	,,	0	360	5	16	None
9	62	M	Acute renal failure due to obstruction and haemolysis after prostatectomy	6	6	Post-operative prophylaxis	30	320	8	12	,,
10	40	M	Crush syndrome	2	3	Prophylaxis	60	600	3 and 15	17	,,

plasma may remain elevated for a long time. With each additional dose the plasma level rises further, and serious toxic effects may appear. The damage sustained by the central nervous system is usually permanent, especially in older patients, and sometimes more incapacitating than the disease for which streptomycin was given (Goodman and Gilman, 1955).

More recently an increasing incidence of toxic effects has been reported as occurring in spite of the smaller doses of streptomycin used currently in clinical practice. A total dose as small as 3 g. in three days has been known to cause vestibular damage, so that a more drastic limitation of dosage, to 0.5 g. daily whenever possible, has been advocated by Cawthorne and Ranger (1957). These authors described 24 cases of streptomycin poisoning, in nine of which urological disorders were present, with impaired renal function in at least two of them. They stressed the danger of giving the drug when there is renal insufficiency, and it would be interesting to know whether abnormalities in renal function could have been detected in all their patients who suffered damage. All of our patients, though only five in number, had gross renal insufficiency. It is an important point, because "on it depends whether the risks of the treatment can be determined beforehand or not" (*Brit. med. J.*, 1957).

Accumulating experiences certainly emphasize the importance of estimating renal function, at least roughly, before giving a course of streptomycin. It would be better to avoid giving it, unless absolutely necessary, when oliguria or shock is present, or when there is a possibility of acute renal failure occurring, as with septic abortions or crush injuries. It would be wise to take further thought and to make a full assessment of renal function before giving streptomycin for specifically renal conditions, or when there is a history of past or present renal disease, or when proteinuria or nitrogen retention is detected. Streptomycin therapy might well be regarded in similar light to the giving of potassium intravenously, where clinicians these days are rather acutely aware of the dangers involved and check that urinary excretion is adequate. Since becoming aware of the importance of asking about the use of streptomycin in anuric patients referred to us we have been surprised by the frequency with which it has been given. Often there has been no clear indication for its use and no awareness of the danger of continuing to administer it during a period of oliguria. The importance of avoiding streptomycin in the treatment of renal failure is not sufficiently well recognized, and finds no mention in recent accounts of the disease (Bull, 1955; Merrill, 1955).

Our own observations confirm the severity of the disability which streptomycin toxicity can induce, but an interesting and important feature is the long period of time which may elapse between administration of the drug and the appearance of symptoms. In both anuric patients symptoms were experienced 28 days after the first dose of streptomycin and 24 days after the treatment was stopped. This delay may be partly attributable to the fact that symptoms are less troublesome while lying in bed. Vestibular damage occurred in both of these men in spite of haemodialysis on the eleventh and sixteenth days and re-establishment of a daily excretion of urine in excess of 1,000 ml. soon after. It is possible that circulating streptomycin was insufficiently removed by dialysis and diuresis and continued to cause damage. Alternatively, the drug could have become fixed in the tissues, or otherwise had time to cause damage which progressed even when streptomycin was removed or at least reduced in concentration.

This matter is not resolved by examining our experiences with other patients in acute renal failure in whom dialysis was deliberately used because they had been given streptomycin. One patient who had received 10 g. of the drug over eight days was not dialysed until the tenth day and yet remained free of symptoms. It must remain for further experience to demonstrate whether dialysis truly helps to prevent the development of vestibular damage due to streptomycin and the limits of safety in regard to dose and delay before dialysis.

There is no doubt, however, that streptomycin can be removed from the blood by dialysis. This fact has not been generally appreciated, and streptomycin could profitably be included in a list of drugs which can be removed by the artificial kidney (Merrill, 1957). Being confined to the extracellular fluid in the body, streptomycin should be more readily removed by dialysis than barbiturates and urea, which are distributed throughout the total body water. There is every reason to believe that early removal by dialysis should assist in preventing vestibular damage, and we now consider the administration of streptomycin in patients with renal failure to be one of the few conditions calling for immediate treatment with an artificial kidney (Edwards and Whyte, 1958).

Summary

Five instances of streptomycin poisoning in patients with renal insufficiency are described. In two of these with acute oliguric renal failure the symptoms of vestibular damage appeared 24 days after the last dose of streptomycin and after diuresis had occurred.

Tests *in vitro* showed that streptomycin can be removed from blood by dialysis, and early treatment with an artificial kidney is recommended for oliguric patients who have been given streptomycin.

Five patients with acute renal failure who had received 1.5 to 10 g. of streptomycin were treated by haemodialysis as early as was possible (three to nine days). None developed signs of toxicity.

Accumulating experience emphasizes the importance of estimating renal function before giving a course of streptomycin.

ADDENDUM.—The Commonwealth Serum Laboratories have kindly agreed to carry out streptomycin assays for us. Tentative conclusions reached for one of our recent patients who had received 3 g. of streptomycin were that dialysis reduced the concentration in the blood from 32 to 17 μg./ml. Unfortunately, this woman developed signs of streptomycin toxicity. She is the only one to have done so of the eight patients who have been treated by dialysis specifically because they had received streptomycin.

REFERENCES

Brit. med. J., 1957, 1, 1466.
Bull, G. M. (1955). *Lancet*, **1**, 731, 777.
Cawthorne, T., and Ranger, D. (1957). *Brit. med. J.*, **1**, 1444.
Edwards, K. D. G., and Whyte, H. M. (1958). *Med. J. Aust.* In press.
Goodman, L. S., and Gilman, A. (1955). *The Pharmacological Basis of Therapeutics*, 2nd ed. Macmillan, New York.
Mackie, T. J., and McCartney, J. E. (1953). *Handbook of Practical Bacteriology*, 9th ed. Livingstone, Edinburgh.
Merrill, J. P. (1955). *The Treatment of Renal Failure*. Grune and Stratton, New York.
—— (1957). *J. chron. Dis.*, **5**, 138.

USE OF SPINAL ANALGESIA IN FORCEPS AND BREECH DELIVERIES

BY

R. T. SEARS, M.A., M.B., F.R.C.S., M.R.C.O.G.
Formerly Registrar, the City Hospital, Nottingham

For many years general anaesthesia has been the anaesthetic of choice for most operative obstetric deliveries, but recent awareness of the danger of inhalation of vomit (Jeffcoate, 1953; Parker, 1954, 1956) has caused concern. The extent of the problem is revealed by reference to the Report on Confidential Inquiries into Maternal Deaths in England and Wales, 1952–4, which shows that inhalation of vomit was responsible for no fewer than 32 of the 49 maternal deaths due to anaesthesia. Recognition of this danger has led, on the one hand, to an increase in the use of local analgesia, and, on the other, to greater precautions when general anaesthesia is administered.

Local analgesia (pudendal block) is undoubtedly safe provided care is taken to avoid overdose; mishaps have been recorded when concentrated solutions have been used (Gordon, 1955; Martin, 1955; Barnes, 1955; Rollason, 1955). Unfortunately, while local analgesia is suitable for most forceps and breech deliveries, it is inadequate for those in which there is difficulty. In order to extend the limits the use of pre-operative intravenous chlorpromazine and pethidine has been advocated. Scott and Gadd (1957) gave 100 mg. of pethidine and 12.5 mg. of chlorpromazine in this way and were able to perform 94% of their forceps deliveries under local analgesia. But this technique may introduce fresh hazards, for there is a risk of apnoea when pethidine is given intravenously in this dosage to a woman who has already had analgesics earlier in labour. The development of such apnoea may be delayed and appear at a time when the patient is unattended.

Although the safety of general anaesthesia has been increased by endeavours to reduce both the incidence of vomit and the risk of inhalation, complete success may not be achieved. The use of apomorphine (J. M. Holmes, 1956) or routine aspiration of the stomach pre-operatively is unpleasant and may be rendered ineffective by subsequent duodenal regurgitation; nor is the provision of tilting labour-ward beds and adequate suction apparatus a complete safeguard. Much depends upon obtaining the services of an anaesthetist skilled in obstetrical anaesthesia, and this is not always possible in the sudden emergencies of obstetric practice.

At a discussion at the Royal Society of Medicine (*Proc. roy. Soc. Med.*, 1957) both the dangers of general anaesthesia and the limitations of local analgesia were appreciated. Little reference was made to the place of spinal analgesia, which has neither the limitations of local analgesia nor the disadvantages of general anaesthesia. For some 25 years it has been the practice in Nottingham to employ spinal analgesia for the majority of caesarean sections, and for the past 20 years it has been used extensively for operative vaginal deliveries. There have been no deaths and no serious complications due to spinal analgesia in the three Nottingham Hospitals admitting maternity cases during this period (H. J. Malkin, 1958, personal communication). I have therefore been encouraged to present the results obtained during the period 1951–5 in 439 cases delivered by the vaginal route at the City Hospital, Nottingham, under spinal analgesia.

Present Series

During the period 1951–5 there were 8,395 deliveries in the City Hospital. These included 391 forceps and 97 breech deliveries requiring anaesthesia. Spinal analgesia was given in preference to other methods of anaesthesia and was used for 371 (95%) forceps deliveries and 68 (70%) breech deliveries. A conservative policy has been practised in the use of forceps, which are rarely employed before one and a half to two hours in the second stage of labour unless there is foetal distress or other abnormality. Of the forceps deliveries 180 were classed as low forceps, 186 as mid-cavity (122 requiring rotation of the foetal head), and 5 as high forceps deliveries.

There were no maternal deaths and, headache excepted, few maternal complications, none of which were serious. The results to the baby were also satisfactory. A "saddle block" technique has been used, 0.8 ml. of 0.5% hyperbaric cinchocaine hydrochloride ("nupercaine") being given. This causes complete loss of sensation in the lower abdomen, perineum, and thighs. Sensation from the uterine cavity is greatly diminished; thus difficult forceps and breech deliveries requiring intrauterine manipulations can be performed without causing distress to the patient. There is complete perineal relaxation, which facilitates delivery and the performance of manipulations such as correction of the malrotated head in forceps deliveries and the bringing down of arms in breech cases.

The conscious patient is able to assist delivery by use of her abdominal muscles; this is valuable in assisted breech deliveries. Nevertheless there is considerable loss of power and the perineal reflex is lost. It is therefore advisable to give the injection as late as possible in breech cases to avoid unnecessary extraction.

Since uterine tone is retained under spinal analgesia the risk of post-partum haemorrhage is reduced, though intravenous ergometrine (0.25 mg.) has been given with delivery of the anterior shoulder in forceps cases and on completion of the second stage in breech deliveries. Post-partum haemorrhage (loss of 20 oz. (570 ml.) or more) occurred in 32 forceps deliveries and one breech (incidence 7.5%), but in 11 cases bleeding was thought to have arisen from cervical or vaginal tears. Manual removal of the placenta was performed in 13 patients (incidence 3%); no undue difficulty was experienced.

Forceps delivery was difficult in five patients who had mitral stenosis, and in three who had chronic bronchitis. Saddle block analgesia was considered especially suitable in these cases.

Reactions of Patient.—Mothers interviewed after delivery under spinal analgesia seem well satisfied by their experience. Patients entering hospital know that spinal analgesia is often used, but no persuasion is attempted if they wish to have another anaesthetic. There was only one refusal in the year 1955; this woman had suffered from headache for two weeks following a diagnostic lumbar puncture some years previously. The placid manner of patients delivered under spinal analgesia is in contrast to the restlessness which is frequently present during delivery under pudendal block.

Contraindications.—Only one patient was encountered in whom spinal analgesia was contraindicated. She was a primigravida of 39 with a major degree of

kyphoscoliosis affecting the lumbar region. She was successfully delivered by forceps under general anaesthesia.

Failures.—Spinal analgesia proved unsuccessful in 13 cases: in six the subarachnoid space was not entered; in seven cerebrospinal fluid was seen to flow, but there was no loss of sensation after the injection was given.

Technique

Great care is taken in the preparation of materials used in the administration of spinal analgesia. Syringes and needles are cleansed, washed in water, and dried to ensure that they are free from extraneous chemicals likely to damage nervous tissue. Syringes, needles, and ampoules of analgesic agents are assembled in a special pack, which is autoclaved in a drum. The contents of the pack comprise: One 5-ml. syringe; one 2-ml. syringe; three lumbar puncture needles (20 S.W.G.); one file for ampoule; one 20-mm. needle; one 16-mm. needle; one ampoule containing 1-ml. of 1% procaine hydrochloride; one ampoule containing 3 ml. of 0.5% cinchocaine hydrochloride in 6% glucose.

The analgesic is given with the patient in either the left lateral or the sitting position, according to the preference of the anaesthetist or the comfort of the patient. If the left lateral is used the patient is inclined on pillows, feet downwards, to limit upward spread of the hyperbaric fluid after its injection. The skin is painted with 0.1% thiomersal, which is allowed to dry to prevent contamination of the lumen of the lumbar puncture needle. Procaine hydrochloride, 1 ml., is used to anaesthetize the skin and subcutaneous tissues of the interspinous space between the third and fourth lumbar vertebrae, and lumbar puncture is performed through this space. After a few drops of clear cerebrospinal fluid have flowed, 0.8 ml. of 0.5% hyperbaric cinchocaine is injected slowly.

Immediately after the injection has been given the patient is sat up in order to limit upward spread of the solution. Two to three minutes later the cinchocaine becomes fixed, and the lithotomy position can be adopted. Sensation is lost within five minutes. The patient is nursed flat for 12 hours and then gradually allowed to sit up.

Foetal Results

The number of cases and the cause of foetal loss in the forceps and breech deliveries are shown in the Table. There were eight foetal deaths which could reasonably be attributed to birth injury among the 371 forceps deliveries, but none was considered to have been caused by analgesia. Similarly the three deaths due to birth injury amongst the 68 breech deliveries were also unrelated to spinal analgesia. The deaths of three babies (one forceps and two breech) were unexplained.

Number of Cases and Cause of Foetal Loss in Forceps and Breech Deliveries, City Hospital, Nottingham, 1951-5

Stillbirths		Neonatal Deaths	
Forceps Delivery (371)			
Intrauterine foetal death	6	Hydrocephalus	1
Congenital abnormalities	2	Intracranial haemorrhage	1
Hydrops foetalis	1	Cause unknown	1
Intracranial haemorrhage	3		
Asphyxia (difficulty in delivery)	4		
Total	16	Total	3
Breech Delivery (68)			
Hydrocephalus	2	Hydrocephalus	1
Asphyxia (difficulty in delivery)	1	Intracranial haemorrhage	2
Cause unknown	1	Cause unknown	1
Total	4	Total	4

There was a noteworthy absence of respiratory difficulty in the surviving babies. Asphyxia livida was present at birth in 20 babies and asphyxia pallida in 7. Factors other than the analgesic—for example, foetal distress *in utero*, difficulty in delivery—were present in 18 of the 27 cases, and may have been responsible for the respiratory difficulty.

Maternal Complications

There have been few complications in this series and none have been serious. But since complications, though rare, constitute such a strong deterrent to the use of spinal analgesia, mishaps which have not occurred in this series are discussed at some length. Evidence is presented that they should be almost eliminated in carefully administered "saddle block" analgesia.

Spinal Shock

There were 10 cases in which the post-partum blood pressure fell to below 100 systolic, but post-partum haemorrhage and trauma to soft parts were thought to be responsible. Each case responded readily to intravenous therapy. There were no cases in which shock could be attributed to the analgesia itself. Nevertheless spinal shock has been responsible for maternal deaths; Klein *et al.* (1953) and Lock and Greiss (1955) report 21 maternal deaths from this cause, but in 17 of these cases caesarean section had been performed and a relatively large dose given.

Spinal shock is a condition of circulatory and respiratory failure probably caused by peripheral vasodilatation and paralysis of respiratory muscles. Respiratory failure is especially apt to occur in the parturient woman because the diaphragm is splinted by the full-term pregnant uterus, and paralysis of the thoracic region of the spinal cord is therefore sufficient to cause respiratory embarrassment. F. Holmes (1957) thinks there is evidence of vena caval obstruction by the uterus in late pregnancy, causing a reduction in venous return to the heart. When spinal analgesia is given, venous return is still further reduced by peripheral vasodilatation. The combination of these two factors he regards as responsible for the special susceptibility to spinal analgesia which some have supposed to exist in the pregnant woman. The risk of spinal shock should therefore be least where peripheral vasodilatation and muscular paralysis are limited to the lumbo-sacral region, as in the saddle block technique using low dosage and a hyperbaric solution.

In order to test the effect on blood pressure of the spinal analgesic administered in cases of forceps delivery a study was made of the records of 68 uncomplicated cases where systolic blood pressure was noted before and shortly after delivery. The blood pressure was unchanged in 22 cases, rose in 20, and fell in 26 cases. In six the fall was as much as 30–40 mm. Hg, but none fell below 100 mm. systolic. These results do not suggest any consistent effect upon blood pressure.

It might also be argued that, although saddle block analgesia does not cause a consistent fall in blood pressure, there may be sufficient effect upon the cardiovascular system to lower the threshold level at which shock develops after blood loss or trauma. As stated above, there were 10 cases in which the blood pressure fell to below 100 systolic following haemorrhage or trauma, but, on the other hand, post-partum

haemorrhages of 30 oz. (850 ml.) or more were sustained in nine patients without signs of shock appearing. There seems no reason to conclude that there is serious lowering of the threshold level at which signs of shock appear.

Meningitis; Headache; Ocular Nerve Palsy

Meningitis.—No case of meningitis has occurred in this series and there has been none in Nottingham since 1939. Meningitis should be avoided by careful technique. It is mentioned in few modern series, though one maternal death is recorded both by Klein *et al.* and by Lock and Greiss; both series cover years when antibiotics were limited.

Headache.—This was a common complication, and 62 (14.1%) patients complained of it. It was mild and did not persist for more than three days in 41 patients, but lasted five days in 16, and persisted for two to three weeks in 5 patients. The headache was throbbing in character and was felt both behind the eyes and over the occiput. It was aggravated by sitting up and was usually relieved by lying prone. Headache was treated by a variety of analgesics, nicotinic acid, and 30% glucose given intravenously. None of these measures was uniformly successful, and the strict maintenance of the prone position appears to be the most effective remedy. A 5–10% incidence of headache following spinal analgesia seems common to most series.

Ocular Nerve Palsy.—One patient, who had severe headache, also had blurring of vision and palsy of the external rectus muscle which persisted for three days. Paralysis of the abducent nerve, diplopia, and transient disturbance of the cerebral cortex have been reported by Macdonald Critchley (1937), Kennedy *et al.* (1950), and Vandam and Dripps (1956). It is probable that these disorders are caused by changes in intracranial tension due to loss of cerebrospinal fluid at the site of lumbar puncture, for they are known to follow diagnostic lumbar puncture (Dattner and Thomas, 1941; Robinson, 1945) and are reversible.

Disturbance of Spinal Cord

Disturbance of the spinal cord is the complication of spinal analgesia which is most feared, since it can reduce a healthy young adult to a helpless cripple, with paralysis of the legs and loss of control of bladder and rectum.

Only one patient developed any disturbance of locomotion; she underwent a difficult rotation of the foetal head and Kielland forceps delivery for foetal distress. A left peroneal palsy developed, and was still present four months after delivery. There was no interference with function of either the bladder or the rectum. Peroneal palsy is a well-recognized complication of forceps delivery, usually attributed to pressure of the foetal head upon the lumbo-sacral nerve, and was probably unrelated to the spinal analgesic given in this case.

Retention of urine occurred in 39 cases (8.9%). Thirty-six were mild and responded to treatment within 48 hours, but in three it persisted for three to seven days. Temporary and partial incontinence of urine, persisting for one week, was observed in two patients; in neither was there retention or infection. Retention of urine is a common complication of forceps delivery conducted under any anaesthesia, and the incidence in this series is not unreasonable. It is possible that incontinence was due to temporary damage to the cauda equina, though such damage usually causes retention of urine.

There were no cases of more serious neurological disorders such as those described by Kennedy *et al.* (1950). Degeneration of the cauda equina and lower levels of the spinal cord (cauda equina syndrome), and chronic adhesive arachnoiditis, are the commonest of these. It is difficult to assess the incidence of these complications since reports are so varied. The clinical picture is described by Macdonald Critchley (1937) and Ferguson and Watkins (1938). In cauda equina syndrome there is loss of sensation over the sacrum and coccyx, anal incontinence, and retention of urine. In severe cases, where damage is more widespread, the legs are involved; there is muscular weakness and serious interference with walking. Damage is usually maximal at the onset and may improve a little in time, but a case of progressive damage leading to death is recorded by Brain and Russell (1937).

Chronic adhesive arachnoiditis produces similar symptoms but arising weeks or months after administration of the analgesic. In this condition damage is produced by ischaemia, and may progress until all the lower segments of the spinal cord are affected. Rosenbaum *et al.* (1952) have emphasized that symptoms may not arise until 6 to 12 months after administration of the analgesic, and may therefore be overlooked in a short follow-up.

The aetiology of both cauda equina syndrome and adhesive arachnoiditis is uncertain. Trauma, infection, chemical impurities, and sensitivity to the analgesic agent have all been suggested. From considerations of the time interval between administration of the analgesic and development of paresis, it is clear that cauda equina syndrome is due to damage sustained at the time of injection, whereas adhesive arachnoiditis is a chronic inflammatory reaction in the meninges. Since cauda equina syndrome does not follow diagnostic lumbar puncture, it is unlikely to be due to damage to the cauda equina by the lumbar puncture needle.

Weston Hurst (1955) has shown that a variety of chemical substances, including antiseptics and detergents, can cause both immediate degeneration of nervous tissue and chronic arachnoiditis when injected into the subarachnoid space of rhesus monkeys. Damage may be done with high dilutions of the substances. In a recent judgment given in the High Court (*The Times*, 1953), it was considered that paralysis following spinal analgesia was caused by contamination of the anaesthetic drug by passage of phenol through minute cracks in the ampoule. Such events may have passed unrecognized in the past. The risk should be avoided by care in the manufacture of anaesthetic solutions, sterilization by autoclave of all materials used, and precautions to ensure that syringes and needles used do not contain impurities.

It is possible that damage may be caused by hypersensitivity to the analgesic drugs. Strong concentrations of analgesic drugs have been shown to cause degeneration of nervous tissue after intrathecal injection in animals (Davis *et al.*, 1931; Macdonald and Watkins, 1937). The concentrations of drugs used were higher than those usually given in humans. Permanent neurological damage is also known to be a rare complication of regional analgesia such as brachial plexus block. In the case of spinal analgesia it is also possible that local factors may sometimes be present within the subarachnoid space and may prevent normal diffusion of the analgesic solution. This would result in an unusually high concentration of analgesic drug. Similar reasoning

has been used by Payne and Bergentz (1956) to explain cases of arachnoiditis which have been found to occur with light cinchocaine analgesia (Hewer, 1933; Thorsén 1947). It therefore seems desirable to use minimal doses in spinal analgesia. Hingson and Hellman (1951), Lock and Greiss (1955), and Mitchell (1955) consider that overdosage may have been responsible for some cases of neurological damage following spinal analgesia. Lock and Greiss recommend that not more than 1.8 mg. of cinchocaine hydrochloride should be used in saddle block analgesia.

Adhesive arachnoiditis has been shown to follow both acute benign lymphocytic meningitis (Barker and Ford, 1937) and cerebrospinal meningitis (Turner, 1948), but there is no convincing evidence to suggest that infection is an aetiological factor in adhesive arachnoiditis following spinal analgesia.

In some instances spinal analgesia appears to activate pre-existing neurological conditions such as disseminated sclerosis or subacute combined degeneration (Macdonald Critchley, 1937; Nicholson and Eversole, 1946). Spinal analgesia should not be used in patients known to suffer from neurological disease.

Discussion

In the American literature, in recent years, large series of cases have been recorded where spinal analgesia has been given without causing either death or serious complications. Gibbs and Cooley (1956) report 12,202 uncomplicated cases in which saddle block analgesia was used for vaginal delivery. Similar series without complications are recorded by Torkelson and Cooley (1951), 4,000 cases; Crowder and McNulty (1951), 1,000 cases; Lewis and Austen (1950), 1,032 cases; and Hundley (1955), 27,925 cases. Dripps and Vandam (1951, 1954) and Vandam and Dripps (1956) quote their experience of 10,098 spinal analgesics given for a variety of operations, including some in the upper abdomen. There were no deaths, and only one case developed serious neurological disorder (subsequently shown to be due to a meningioma) within a follow-up period of between six months and five years. Minor neurological disorders were, however, more frequent: 66 patients showed transient sensory and motor changes in the legs and 34 had temporary visual disturbances.

Low spinal analgesia has several advantages. Good operating conditions are produced, and there is no depression of the foetal respiratory centre. The technique is easy to learn and there are few failures. In an emergency the analgesic can be administered by the obstetrician. The absence of serious complications in this series and in the much larger ones reported in the U.S.A. shows that the fear of unpleasant sequelae of spinal analgesia can be exaggerated. Since only a saddle block is required for forceps and breech delivery the danger of spinal shock is minimal. The use of careful technique and low dosage reduces the risk of serious neurological damage.

Few would dispute the present-day preference for the use of general anaesthesia in most surgical operations, but there is room for second thoughts in the limited field of anaesthesia for forceps and breech deliveries which cannot reasonably be conducted under local analgesia. Here some complications inherent in general anaesthesia occur more often than usual, whereas those of spinal analgesia are reduced, since only a saddle block is used. The incidence of serious complications is probably less with spinal analgesia than with general anaesthesia, particularly if the latter has to be administered in an emergency by an unskilled anaesthetist. Low spinal analgesia is therefore worthy of serious consideration for difficult forceps and breech deliveries.

Summary

371 forceps and 68 breech deliveries were conducted under spinal analgesia in the City Hospital, Nottingham, during the years 1951 to 1955.

There were no maternal deaths and no serious post-analgesic complications.

Headache occurred in 14.1% of patients.

There were 20 stillbirths and 7 neonatal deaths, but these included 15 babies who had congenital abnormalities or died *in utero*, and none were attributed to spinal analgesia.

The advantages of spinal analgesia for forceps and breech deliveries that cannot be performed under local analgesia are discussed.

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REFERENCES

Barker, L. F., and Ford, F. R. (1937). *J. Amer. med. Ass.*, **109**, 785.
Barnes, J. E. M. (1955). *Brit. med. J.*, **2**, 677.
Brain, R., and Russell, Dorothy (1937). *Proc. roy. Soc. Med.*, **30**, 1024.
Critchley, M. (1937). Ibid., **30**, 1007.
Crowder, R. C., and McNulty, J. V. (1951). *Ann. west. Med. Surg.*, **5**, 531.
Dattner, B., and Thomas, E. W. (1941). *N.Y. J. Med.*, **41**, 1660.
Davis, L., Haven, H., Givens, J. H., and Emmett, J. (1931). *J. Amer. med. Ass.*, **97**, 1781.
Dripps, R. D., and Vandam, L. D. (1951). Ibid., **147**, 1118.
—— —— (1954). Ibid., **156**, 1486.
Ferguson, F. R., and Watkins, K. H. (1938). *Brit. J. Surg.*, **25**, 735.
Gibbs, C. E., and Cooley, C. L. (1956). *West. J. Surg.*, **64**, 76.
Gordon, J. (1955). *Brit. med. J.*, **2**, 489.
Hewer, C. L. (1933). *Proc. roy. Soc. Med.*, **26**, 506.
Hingson, R. A., and Hellman, L. M. (1951). *Anesthesiology*, **12**, 745.
Holmes, F. (1957). *J. Obstet. Gynaec. Brit. Emp.*, **64**, 229.
Holmes, J. M. (1956). Ibid., **63**, 239.
Hundley, J. M., jun. (1955). *Amer. J. Obstet. Gynec.*, **70**, 872.
Hurst, E. W. (1955). *J. Path. Bact.*, **70**, 167.
Jeffcoate, T. N. A. (1953). *Brit. med. J.*, **2**, 951.
Kennedy, F., Effron, A. S., and Perry, G. (1950). *Surg. Gynec. Obstet.*, **91**, 385.
Klein, M. D., Clahr, J., Tamis, A. B., and Solkow, M. L. (1953). *N.Y. J. Med.*, **53**, 2861.
Lewis, M. S., and Austin, R. B. (1950). *Amer. J. Obstet. Gynec.*, **59**, 1146.
Lock, F. R., and Greiss, F. C., jun. (1955). *Ibid.*, **70**, 861.
Macdonald, A. C., and Watkins, K. H. (1938). *Brit. J. Surg.*, **25**, 879.
Martin, W. I. (1955). *Brit. med. J.*, **2**, 676.
Mitchell, R. McN. (1955). *Obstet. and Gynec.*, **5**, 123.
Nicholson, M. J., and Eversole, U. H. (1946). *J. Amer. med. Ass.*, **132**, 679.
Parker, R. B. (1954). *Brit. med. J.*, **2**, 65.
—— (1956). Ibid., **2**, 16.
Payne, J. P., and Bergentz, S. E. (1956). *Lancet*, **1**, 666.
Proc. roy. Soc. Med., 1957, **50**, 547.
Robinson, H. M., jun. (1945). *Amer. J. Syph.*, **29**, 422.
Rollason, W. N. (1955). *Brit. med. J.*, **2**, 677.
Rosenbaum, H. E., Long, F. B., Hinchey, T. R., and Trufant, S. A. (1952). *A.M.A. Arch. Neurol. Psychiat.*, **68**, 783.
Scott, J. S., and Gadd, R. L. (1957). *Brit. med. J.*, **1**, 971.
The Times, Law Report, November 13, 1953.
Thorsén, G. (1947). *Acta chir. scand.*, 95, Suppl. 121.
Torkelson, H. P., and Cooley, C. L. (1951). *West. J. Surg.*, **59**, 533.
Turner, J. W. A. (1948). *Lancet*, **1**, 398.
Vandam, L. D., and Dripps, R. D. (1956). *J. Amer. med. Ass.*, **161**, 586.

PUDENDAL NERVE BLOCK

BY

P. A. S. SAHAY, M.B., B.S., B.Sc.

Registrar in Obstetrics and Gynaecology, General Hospital, Halifax

With the passing of the high-forceps operation into obsolescence and reduction of the incidence of the so-called difficult mid-forceps operations, vaginal deliveries are now much safer. An important outcome has been the removal of the obvious objection to the employment of pudendal block as a routine and preferred form of analgesia for a great majority of vaginal deliveries, for which otherwise one would use general anaesthesia, with an occasional fatality. The objection on grounds of inadequacy is therefore no longer justified. General anaesthesia administered by a properly trained anaesthetist to a properly prepared patient is an ideal less commonly attained in obstetric emergencies. The obstetrician's usual preference for the lithotomy position for difficult manipulations, lack of delivery tables with emergency head-low tilting mechanism, and hence the risk of accidental aspiration of vomit, are discouraging problems without, as yet, an acceptable solution. The increasing popularity of pudendal block in this country and elsewhere is therefore a very welcome trend in modern obstetrics.

At the Halifax General Hospital, during a 14-months period ending January 31, 1958, it has been possible, by adopting a simple routine, combining parenteral pethidine hydrochloride and self-administered trichlorethylene ("trilene") with pudendal block, to reduce considerably the number of cases requiring general anaesthesia for operative vaginal deliveries. General anaesthesia was, however, used for all breech extractions and on occasion when preferred by the other members of the staff. Whereas previously the use of pudendal block was limited to occasions according to individual personal preferences, during the period under review an effort was made to employ this method when at all possible.

Technique

The patient is put in the lithotomy position. To block the pudendal nerve as it passes dorsal to the spine just before entering Alcock's canal, the middle and index fingers are placed in the vagina to palpate the ischial spine; a 6-in. (15-cm.) pudendal needle fitted to an all-glass 20-ml. syringe containing 1% procaine hydrochloride solution, is guided through the perineum, entering at a point midway between the anus and the ischial tuberosity, to reach the inferior border of the spine. From here it is guided to its posterior surface and beyond, to reach the superior border and finally a point roughly 2 cm. above it. Five ml. of the procaine solution is injected at this point; the needle is then slightly withdrawn and a further 3 ml. is injected posterior to the spine, and finally 2 ml. at the inferior border of the spine. The needle is partially withdrawn and directed laterally to the ischial tuberosity, and 5 ml. is injected there to anaesthetize the perineal branches of the posterior femoral cutaneous nerve. To block the anterior labial branches of the ilio-inguinal nerve, the needle is again partially withdrawn and redirected anteriorly and superficially in the fold of the labium majus to a point slightly above the level of the clitoris, the remaining 5 ml. is then injected as the needle is gradually and finally completely withdrawn. The same procedure is repeated on the other side.

Always, before the actual injection, accidental entry into a blood vessel is ruled out, or a slight readjustment of the needle is made so that no blood enters the syringe on withdrawal of the plunger. With this method of approach, the needle is in close proximity to the pudendal nerve and the accompanying blood vessels are almost invariably pierced. This is quite a reassuring sign, and all that is then necessary is a slight medial readjustment of the needle. Pethidine hydrochloride, 50 mg., is now injected slowly into a vein, and another 50 mg. intramuscularly. Roughly three to five minutes is allowed for the development of perineal anaesthesia, which is as a rule verified by checking the cutaneous sensation before proceeding with the episiotomy or the delivery. When pains are felt the patients are allowed to self-administer trichlorethylene, its use thus being limited to obtaining analgesia during the uterine contractions. Training in the use of this technique is easy: even the junior house officers achieve success at a single attempt.

TABLE I.—*Deliveries under Pudendal Block*

Group	Forceps Deliveries				Assisted Breech Deliveries		Episiotomies		Total
	Scanzoni Manœuvres	Rotations	Face	Others	Forceps	Others	Face	Others	
A	3	17	1	27	1	14	2	12	77
B	0	3	0	14	4	3	0	1	25
Total	3	20	1	41	5	17	2	13	102

Results

During the period under review 102 cases were delivered under pudendal block (Table I). Out of these, 77 were conducted either by me personally or by the house officer under my direct supervision, and in all these cases the above-described technique was followed strictly. An analysis of the cases is given in Table I under Group A. There were 48 forceps deliveries. Of these, 20 required either manual or forceps rotation; there was one face presentation; and the other 27 were vertex presentations in which the indications for forceps included the following: (*a*) distress, either maternal or foetal; (*b*) inertia; (*c*) prophylactic for delay in the second stage or maternal indications such as heart disease. Assisted breech deliveries numbered 15, one of which required forceps to the after-coming head. In the remaining 14, thought to be due to delay in the second stage, forceps application was indicated, but after liberal episiotomy and voluntary efforts of the patient spontaneous delivery occurred. In these cases, excluding of course those in which the foetal heart was known to be absent, the babies cried instantaneously after birth, on many occasions even before the cord could be clamped and cut. The other 25 cases have been placed separately in group B, because in those instances possibly the injection of pethidine was omitted and some minor deviations from the described technique could not be ruled out.

In the same period, after excluding breech extractions, either alone or preceded by internal version, 52 patients were delivered under general anaesthesia (Table II).

These included 46 forceps and 6 assisted breech deliveries. Of the 154 probable cases, therefore, only 52 were actually subjected to general anaesthesia. Considering that no attempt was made to influence

TABLE II.—*Deliveries under General Anaesthesia*

Forceps Deliveries			Assisted Breech Deliveries			Total
Rotations	Others	Total	Forceps	Others	Total	
12	34	46	4	2	6	52

individual preferences in favour of pudendal block, the reduction in the incidence of avoidable general anaesthesia by 66.2% in this period can be regarded as encouraging.

Discussion

Lately some interest has been focused on the technique of transvaginal pudendal nerve block (Kobak, Evans, and Johnson, 1956; Leshock, 1957). This would appear to be a simple and perhaps preferable approach, since the injection is given direct through the vaginal wall, at the posterior surface of the spine and above in the sacrosciatic notch—a procedure which ensures complete blocking of the pudendal nerve even if it divides higher up above the spine, as it often does. Unfortunately this does not take into account the anterior labial branches of the ilio-inguinal nerve and the perineal branches of the posterior femoral cutaneous nerve. Also it is not always possible to use the transvaginal technique owing to lack of space, and occasionally more than one attempt may be necessary to achieve a block (Kobak, Evans, and Johnson, 1956). As a routine procedure, therefore, it is desirable to adhere to the transperineal route and inject at all the three sites as described, through a single entry on each side. Use of a point midway between the ischial tuberosity and the anus as the site of entry has the advantage of bringing the posterior surface of the ischial spine and the point 2 cm. above its superior border within direct and easy reach of the 6-in. (15-cm.) pudendal needle. This point also happens to be very conveniently placed in relation to the remaining two sites of injection.

This technique does not include local infiltration of the perineal skin, and thus there is no artificial oedema of the tissues to make any repair work difficult. The conspicuous absence of vulval and vaginal haematomas from the present series of cases makes one wonder whether or not, in the few instances where they are said to appear following transperineal pudendal block, the cause lies entirely in the traumatic nature of the deliveries, forceps or otherwise.

Even a single dose of 100 mg. of pethidine may raise the pain threshold by 50% (Bourne and Williams, 1948a). To use this drug with advantage to enhance the effectiveness of pudendal block analgesic one would require to use it reasonably close to the time of the delivery, a procedure which is generally in disfavour. It has been shown that up to 30 minutes after birth the oxygen saturation in the arterial blood of infants, born of mothers receiving 100 mg. of pethidine hydrochloride and 0.4 mg. of scopolamine within two to four hours of delivery, remains significantly low when compared with those in the control group (Taylor *et al.*, 1955). This measurable depression in the blood oxygen level was, however, not thought to be injurious. The use of pethidine in doses varying from 100 mg. to 400 mg. or more during labour is very common. To counteract the possible depressant effect on the respiration of the baby, intravenous injection of 10 mg. of nalorphine hydrobromide given to the mother about five minutes before the delivery has been recommended (Bourne and Williams, 1958). Unfortunately it also neutralizes the analgesic action of pethidine (Micks, 1957). In the routine described in the present paper, a slow injection of 50 mg. of pethidine hydrochloride is given intravenously while still waiting for the perineal analgesia to develop. The desired effect is achieved immediately. The birth of the baby usually takes place within five to seven minutes after the injection. The babies in the cases reported under group A (Table I) did not show any clinical evidence of respiratory depression; on the contrary, many of them, even in the presence of foetal distress, cried spontaneously. The intramuscular injection of 50 mg. of pethidine, given at the same time, assures the prolongation of the drug's beneficial action throughout the time required for repair of the episiotomy; it also provides rest and sedation in the immediate post-partum period. In the 77 cases (Table I, group A), no ill-effects of intravenous administration of pethidine were noted. The fear of sudden fall in blood pressure after intravenous pethidine (Holland and Bourne, 1955) is not substantiated.

Self-administered trichlorethylene, when used for analgesia in labour, does not affect the oxygen saturation of the baby's arterial blood (Taylor *et al.*, 1955). The patients are therefore allowed the benefit of its use by the usual method.

The proper choice of analgesic agent for pudendal block is equally important. A total of 40 ml. of 1% lignocaine hydrochloride is not only quite safe but also very effective and speedy, and has wonderful spreading properties. Gross overdosage of lignocaine, however, is not easily tolerated, and death following such overdosage has been reported (Lock and Greiss, 1955). It is nearly twice as toxic as procaine. For beginners, therefore, the importance of caution in the matter of dosage cannot be stressed enough. In this series, 40 ml. of 1% procaine hydrochloride was employed for the block. Using plain procaine, one is at the slight disadvantage of having to wait three to five minutes for the analgesia to develop. This is usually remedied by adding hyaluronidase, which increases its spreading properties. Procaine when used with hyaluronidase alone produces a very short-lasting analgesia (Kobak, Evans, and Johnson, 1956), but the addition of 1:1,000 adrenaline (0.5 ml. adrenaline to 30 ml. of procaine) produces a comparatively long-lasting analgesia (Kobak, Evans, and Johnson, 1956). Addition of even minute quantities of adrenaline as above may produce a marked adrenaline effect characterized by complete cessation or otherwise weakening of uterine contraction and tone, lasting for as long as 20 minutes (Woolsey, 1955). The resulting period of uterine inertia following the use of adrenaline in the procaine–hyaluronidase mixture requires recognition if haemorrhage caused by detachment of the placenta before the return of the uterine tone is to be avoided. A wait of 20 minutes for the return of the uterine tone before attempting to deliver may cost the life of the baby, which in a sudden case of foetal distress is the very thing one is trying to prevent.

Use of trichlorethylene, self-administered during labour, is an established and safe practice, but the drug sometimes causes cardiac arrhythmias, and when in combination with adrenaline may give rise to ventricular

fibrillation (Bourne and Williams, 1948b; Lock and Greiss, 1955). This may hold true also if, after an initial pudendal block with procaine–hyalase–adrenaline mixture, it becomes necessary to administer general anaesthesia in an emergency. Plain procaine was therefore considered to be a safer agent to use in the cases above. An effective pudendal block, achieved in this way, assures one of the co-operation of the mother, who in most instances is thrilled to have actively participated in the birth of her child and is glad to be able to see and hear her baby cry for the very first time.

Summary and Conclusions

A technique for pudendal nerve block anaesthesia for routine use is described.

Cases delivered under pudendal block and those under general anaesthesia are recorded and analysed.

An unconventional use of pethidine hydrochloride and self-administered trichlorethylene as an adjunct to pudendal block is described and discussed.

A critical study of local analgesic agents commonly used for this purpose has been made.

It is concluded that 40 ml. of 1% procaine hydrochloride (plain), injected according to the technique described above, produces a satisfactory pudendal nerve block and perineal analgesia; also that the perineal analgesia so developed, when combined with the use of pethidine and self-administered trilene analgesia, permits most of the operative vaginal deliveries to be carried out without general anaesthesia.

ADDENDUM.—Since the preparations for this paper were completed, 40 ml. of 1% lignocaine hydrochloride has been substituted in place of procaine. It is perhaps a very premature observation at this stage, but it appears that so far it has lived up to its reputation, and lignocaine, when used with proper caution, may prove to be better than procaine. It is more potent and produces a more prompt and extensive analgesia. It is as safe as procaine if the strength of 1% is not exceeded. While 2% procaine may in some instances be used for nerve blocks, lignocaine in this strength should on no account be used for pudendal block.

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REFERENCES

Bourne, A. W., and Williams, L. H. (1948a). *Recent Advances in Obstetrics and Gynaecology*, 7th ed., p. 89. Churchill, London.

—— —— (1948b). Ibid., 7th ed., p. 106.

—— —— (1958). Ibid., 9th ed., p. 187.

Holland, Sir E., and Bourne, A. (1955). *British Obstetrics and Gynaecological Practice: Obstetrics*, p. 1045. Heinemann, London.

Kobak, A. J., Evans, E. F., and Johnson, G. R. (1956). *Amer. J. Obstet. Gynec.*, **71**, 981.

Leshock, J. C. (1957). Ibid., **74**, 1128.

Lock, F. R., and Greiss, F. C., jun. (1955). Ibid., **70**, 861.

Micks, R. H. (1957). *The Essentials of Materia Medica, Pharmacology and Therapeutics*, 7th ed., p. 31. Churchill, London.

Taylor, E. S., Fumetti, H. H. von, Essig, L. L., Goodman, S. N., and Walker, L. C. (1955). *Amer. J. Obstet. Gynec.*, **69**, 348.

Woolsey, E. L. (1955). Ibid., **69**, 131.

MANIFESTATIONS AND AETIOLOGY OF HYPERTENSION IN THE COLOURED AND BANTU

BY

B. N. FRASER, M.B., M.R.C.P.Ed.
Coronation Hospital, Johannesburg

Hypertension is known to be common in the Bantu in South Africa. A survey was made among both urban and country Bantu by Ordman (1948), who found a significant proportion with a systolic blood pressure of over 150 mm. Hg and a diastolic over 90 in all age groups, though there was a sharp drop in incidence of high blood pressure in males over the age of 60.

Comstock (1957) carried out a survey among both Whites and Negroes in the Southern United States, and his figures showed that the average blood-pressure readings, both systolic and diastolic, are higher in the American adult Negro than his white counterpart. Lennard and Glock (1957), in an appraisal of the distribution of hypertension among Negroes and Whites in the United States, stated that all studies support the conclusion that Negroes more often have essential hypertension, hypertensive heart disease, hypertensive cardiovascular disease or related disorders, than Whites.

Reports from other parts of Africa other than South Africa have revealed variable results. Gelfand (1957) stated that in Rhodesia hypertension, both essential and secondary to chronic nephritis, is common, but he was unable to decide whether it was as frequent as, less frequent, or more frequent than in the white population. He felt comparison between the two races was difficult, since the Europeans' expectation of life is on the whole much higher.

Donnison's (1929) investigation of the blood pressure of males among tribes in the highlands of Kenya showed that up to the fourth decade the average blood pressure was similar to that of European males, but that thereafter there was a tendency to lower pressures. Williams (1944) stated that the majority of cases seen by him in Uganda were secondary to nephritis and urethral stricture. He considered essential hypertension to be rare.

It was decided to investigate hypertension among Bantu and Coloured in-patients as regards incidence, aetiology, morbidity, and mortality. Cases admitted to one of the two medical units at Coronation Hospital during the period January 1, 1955, to December 31, 1956, were used for this purpose. However, owing to the infrequency with which permission was obtained for post-mortem examination, a longer period was taken for investigating necropsy material as regards the incidence of underlying renal disease. The figures of 140 mm. Hg systolic and 90 mm. Hg diastolic were taken as the dividing line between raised and normal blood pressure. This was perhaps not as desirable as relating the blood-pressure reading of each case to a figure taken from a table showing the average blood pressure for that age and sex group, as has been suggested by Pickering (1955). However, no such tables have been compiled for the South African Bantu and Coloured. Comstock's (1957) survey in America has shown that in all age groups the average blood pressure is higher in the American Negro, and the same might well apply to the South African Bantu. Also in many of the Bantu

cases the exact age is uncertain, though this would not necessarily make much difference to a sex-and-age adjusted score. Indian and Chinese cases were excluded from the survey as there were too few to merit inclusion.

Age of Presentation

Table I shows the number of Bantu and Coloured patients admitted during the period of study, with the numbers and percentages of cases presenting with persistent benign hypertension, malignant hypertension, and non-persistent hypertension. It will be seen from the percentage figures that the peak age of presentation of patients with benign hypertension, in both sexes, is over 60, and that there is a tendency for female cases to show themselves at an earlier age than males. Although it is striking that many of the cases present at an early age, there is no doubt that the shorter longevity of the non-European as compared with the European contributes to the impression that hypertension occurs at an earlier age in the former than in the latter. It will be noted that there are fewer total admissions in the 50–59 and the 60-and-over age groups than in the younger age groups. If more non-Europeans lived to a later age, then more would present in this period of life.

TABLE I.—*All Bantu and Coloured Cases (January 1, 1955, to December 31, 1956). Deaths to December 31, 1957*

Age	No. of Cases	Cases with Persistent Benign Hypertension		Cases with Malignant Hypertension		Cases with Non-Persistent Hypertension		Deaths with Hypertension
		No.	%	No.	%	No.	%	
Males								
Under 20 ..	92	—	—	—	—	—	—	—
20–29 ..	236	2	0·8	1	0·4	2	0·8	—
30–39 ..	331	16	4·8	1	0·3	4	1·2	5
40–49 ..	252	15	6	3	1·2	2	0·8	6
50–59 ..	201	25	12·4	0	—	7	3·5	8
60 and over	172	34	19·8	1	0·6	6	3·5	15
Total ..	1,284	92	7·2	6	0·5	21	1·6	34
Females								
Under 20 ..	94	2	2·1	—	—	—	—	1
20–29 ..	220	5	2·3	—	—	3	1·4	1
30–39 ..	195	21	10·8	3	1·5	6	3·1	5
40–49 ..	174	27	15·5	6	3·4	10	5·7	6
50–59 ..	110	17	15·6	2	1·9	2	1·9	7
60 and over	115	27	23·5	2	1·7	12	10·4	12
Total ..	908	99	10·9	13	1·4	33	3·6	32

The peak age of presentation of symptoms in Europeans is reported by Søbye (1948) to be 60–64 in men and 65–69 in women with benign hypertension. It is apparent that the European and non-European are alike in presenting late in life. Søbye gives the age group 50–54 as being the main one for presentation of symptoms in both European men and women with malignant hypertension. Our figures are too small for comparison, though malignant hypertension would appear from our few cases to occur at an earlier age in the non-European than benign hypertension.

Presenting Symptoms and Cause of Death

In Table II are shown the main presenting features of the cases with persistent hypertension. It will be seen that the main causes of death are cardiac failure, cerebral accidents, and uraemia in about equal proportions. This contrasts with the findings in European cases, where the figures given by various authors vary but are approximately 50% heart disease, 25% cerebrovascular accidents, and 10% uraemia. The lower incidence of deaths due to cardiac failure in the non-European is probably due to the infrequency of coronary artery disease. Coronary artery disease and thrombosis is almost unknown in the Bantu. The incidence is higher in Coloureds, though not nearly as high as in Europeans. Only one of our cases—a Coloured female—had definite myocardial infarction. The higher incidence of uraemia is attributed to the prevalence of primary renal disease.

TABLE II.—*Main Presenting Symptoms and Causes of Death in Cases with Persistent Hypertension*

	Males		Females		Total	
	No.	Deaths	No.	Deaths	No.	Deaths
Congestive cardiac failure ..	43	12	47	4	90	16
Cerebrovascular symptoms	26	9	30	14	56	23
Renal symptoms and uraemia	17	11	16	8	33	19
Diabetes	3	—	8	—	11	—
Epistaxis	5	—	7	—	12	—

Sex Incidence and Mortality

Excluding readmissions, 264 cases with hypertension were admitted to the unit during the years 1955 and 1956—in all, 12% of the total number of Bantu and Coloured patients admitted during this period. Of these, 66 patients died before the end of 1957, accounting for just over 25% of all deaths (see Table III). Although far fewer Bantu females were admitted than males, there were slightly more who had hypertension. There are two reasons for the greater number of admissions of Bantu males. A census carried out in 1950 in three areas adjacent to the hospital, from which large numbers of patients are drawn, showed a total population of 66,577 Bantu. Over the age of 14, 54.5% of this population were males and 45.5% females. In addition, the number of medical beds available in the hospital for adult Bantu female patients is half that available for males. Consequently a tighter control is exercised over female medical admissions. The Coloured population in the area of the hospital is thought to be more or less equal as regards the sexes and an equal number of medical beds is available for male and female patients, so that the number of admissions of both sexes is about equal. However, far more Coloured females were admitted with hypertension than Coloured males. Although the mortality rate of the non-European female is slightly lower than that of the male, the greater incidence results in at least as many deaths, and the conspicuously better prognosis found in European women with hypertension as compared with European men is certainly not evident in the Bantu and Coloured.

TABLE III.—*All Cases, January 1, 1955 to December 31, 1956. (Deaths to December 31, 1957)*

	African Males		African Females		Coloured Males		Coloured Females		Total	
	No.	Deaths	No.	Deaths	No.	Deaths	No.	Deaths	No.	Deaths
Cases without hypertension ..	1,019	93	622	65	146	18	131	17	1,928	193 (10%)
Cases with hypertension ..	94	25	105	22	25	9	40	10	264	66 (25%)
All cases									2,192	259 (12%)

In 54 of the cases the raised blood pressure was not sustained, dropping to normal levels within a period of

a few days to two weeks. The death rate was lower in this group than in the group with persistent hypertension, and it approximated the rate for cases without hypertension. The more severe grades of hypertension were, as to be expected, associated with a higher mortality rate (see Table IV).

TABLE IV.—*Cases of Hypertension According to Their Degree of Severity*

Degree of Severity	No. of Cases	Deaths
Non-persistent	54	6 (11%)
Mild	74	15 (20%)
Moderate	79	17 (22%)
Severe	30	13 (43%)
Gross	8	5 (62%)
Malignant	19	10 (53%)

Mild = General trend of diastolic pressure between 90 and 110 mm. Hg. Moderate = Between 110 and 125 mm. Hg. Severe = Between 125 and 140 mm. Hg. Gross = Over 140 mm. Hg. Malignant = Hypertension + papilloedema.

Aetiology

Apart from the very rare case in which the patient died within a few hours of admission, microscopical examination of the urine was carried out, often on several occasions, as well as frequent testing for albumin and specific gravity. Biochemical examination of the blood—urea, chloride, sodium, potassium, and carbon dioxide combining power—was done as a routine. Where considered necessary, estimation of serum cholesterol and the protein fractions was carried out, as well as any other laboratory investigation that was indicated. In many cases, especially where a kidney lesion was suspected, intravenous pyelography and cystoscopy with retrograde pyelography was undertaken. It is often very difficult to judge whether a case is primarily renal or not. Bechgaard (1946) has pointed out that this is particularly difficult in elderly European women where hypertension, nephrosclerosis, and cystitis often occur together, as elevation of the blood pressure, pyuria, and some derangement of renal function in these patients could easily lead to a false diagnosis of a primary chronic pyelonephritis.

In the non-European group studied, contrast radiography and operative procedures demonstrated two cases of bilateral hydronephrosis, two of renal stone, and one each of double ureter, bilateral bifid pelves, and unilateral hypoplastic kidney. In all, of the 264 cases 70 were diagnosed on radiological, operative, necropsy, and clinical grounds as being primarily renal in origin. This impression that there was a high incidence of underlying renal disease was strengthened by necropsy results. Permission for necropsy was unfortunately obtained in only a minority of patients who were admitted to the unit between January 1, 1951, and December 31, 1956, and who died before January 1, 1958—47 cases in all. Twenty-one cases showed underlying renal disease other than nephrosclerosis. Two cases showed prostatic hypertrophy with bilateral hydronephrosis, and there were two with chronic glomerulonephritis. There was one case of diabetic glomerulosclerosis, and another diabetic revealed glomerulosclerosis and necrotizing papillitis. The remaining 15 cases showed chronic pyelonephritis, in two the process was focal.

Necropsy figures given by other authors have shown a high incidence of underlying renal disease in cases of hypertension in the non-European in Johannesburg. Becker (1943), Uys (1953), and Levin (1957) quote figures compiled from the necropsy material of the pathology department of the University of the Witwatersrand Medical School. Becker stated that of 247 necropsies done on Coloureds and Bantus with hypertension between 1924 and 1938, 40% were nephrogenous. Uys reviewed 3,707 consecutive Bantu necropsies from 1940 to 1951; of these, 800 had renal disease. There were 76 cases of hypertension nephrosclerosis (23 of these, malignant nephrosclerosis) and 71 cases showed hypertension with underlying kidney disease. Of these 71 cases, 42 showed glomerulonephritis, 18 pyelonephritis, and 8 hydronephrosis. Levin, in a more recent review, stated that of 398 consecutive necropsies in the non-European, 54 showed evidence of hypertension, of which 34 were essential and 18 secondary to chronic pyelonephritis. In none of our cases was an endocrine cause found, though appropriate clinical and laboratory tests were instituted if any indication existed; nor was any found at necropsy. Coarctation of the aorta was not present in any case.

Electrocardiographic Changes

Electrocardiography was performed in the majority of cases. Table V shows the changes found. It will be noted that, even in the milder group, the electrocardiogram often showed changes suggesting left ventricular preponderance. Gillanders (1951) found that the electrocardiogram often showed left ventricular hypertrophy and a horizontal position of the heart in cases of malnutrition heart disease, and this may account in part for the changes found in the cases with mild or non-persistent hypertension, where the raised blood pressure may have played only a minor part in the electrocardiographic changes, especially as many of these cases were in cardiac failure. In Europeans electrocardiographic changes are not a feature of hypertonia (uneventful blood pressure).

TABLE V.—*Electrocardiographic Changes*

Group	Total	L.A.D.	V.	H.	L.V.H. and L.V.S.	L.V.H.	L.V.S.	L.B.B.B.	R.B.B.B.	Abnormal Rhythm
Non-persistent ..	52	35	10	7	11	3	8	3	—	9
Mild	69	37	16	16	9	8	9	2	—	10
Moderate to malignant ..	124	89	15	20	38	8	37	4	1	14

L.A.D. = Horizontal heart with left axis deviation in standard leads.
V. = Vertical heart.
H. = Horizontal heart with no left axis deviation in standard leads.
L.V.H. = Left ventricular hypertrophy; where one or more of the following features present: R in lead V_5 or V_6 greater than 25 mm.; S in lead V_1 + R in lead V_5 greater than 35 mm.; R in lead aVL 13 mm. or more tall where lead aVL showed a left ventricular pattern; R in lead aVF 20 mm. or more tall where lead aVF showed a left ventricular pattern.
L.V.S. = Left ventricular strain: T-wave inversion ± depressed S.T. segments in one or more left ventricular leads.
L.B.B.B. = Left bundle branch block.
R.B.B.B. = Right bundle branch block.
Abnormal rhythm = Auricular extrasystoles 3, ventricular extrasystoles 21, auricular fibrillation 5, auricular flutter 1, auricular flutter—fibrillation 1, transient auriculo-ventricular dissociation 1, paroxysmal ventricular tachycardia 1.

Summary

A study among Coloured and Bantu in-patients reveals that hypertension and its complications are a common cause of admission and that these cases carry a high mortality. Females are more often affected than males. Renal disease is a common underlying cause. Compared with the European, hypertension presents at a similar age, but is more serious in the female, and the cause of death is more evenly distributed between heart failure, cerebrovascular accidents, and uraemia.

Endocrine causes are rare. Electrocardiographic changes are found commonly even among the milder cases.

My thanks are due to Dr. G. D. Elliott, medical superintendent of Coronation Hospital, for permission to publish, and to Dr. S. Grieve, senior physician, for the use of clinical material in his wards and for much encouragement and advice. I would also like to thank Professor B. J. P. Becker, of the pathology department of the University of the Witwatersrand Medical School, for permission to publish necropsy findings; and Dr. M. E. Davenport, of the *x*-ray department of Coronation Hospital, Dr. R. Cassel and Miss J. Horn, of the South African Institute for Medical Research, and Mr. C. D. Kisner, who performed the urological investigations.

REFERENCES

Bechgaard, P. (1946). *Acta med. scand.*, Suppl. 172.
Becker, B. J. P. (1943). Cardiovascular Disease in the Bantu and Coloured Races of South Africa. M.D. Thesis, University of the Witwatersrand.
Comstock, G. W. (1957). *Amer. J. Hyg.*, **65**, 271.
Donnison, C. P. (1929). *Lancet*, **1**, 6.
Gelfand, M. (1957). *The Sick African*, 3rd ed. Juta, Johannesburg.
Gillanders, A. D. (1951). *Brit. Heart J.*, **13**, 177.
Lennard, H. L., and Glock, C. Y. (1957). *J. chron. Dis.*, **5**, 186.
Levin, N. W. (1957). *Leech (Johannesburg)*, **27**, 29.
Ordman, B. (1948). *Clin. Proc.*, **7**, 183.
Pickering, G. W. (1955). *High Blood Pressure*. Churchill, London.
Søbye, P. (1948). *Heredity in Essential Hypertension and Nephrosclerosis*. Munksgaard, Copenhagen.
Uys, C. J. (1953). Renal Disease in the Bantu. M.D. Thesis, University of the Witwatersrand.
Williams, A. W. (1944). *E. Afr. med. J.*, **21**, 328.

TREATMENT WITH CORTISONE OF HAEMORRHAGIC DISEASE DUE TO A CIRCULATING ANTICOAGULANT

BY

W. M. R. HENDERSON, M.D.
Pathologist, Pembury Hospital, Tunbridge Wells, Kent

Reports of haemophilia-like disease due to circulating anticoagulants are still comparatively rare, though they have become more frequent since the introduction of the thromboplastin generation and other sensitive tests which help to distinguish these cases from true haemophilia or Christmas disease. Two cases have, however, been seen in this hospital within a period of three years. The first, in an old lady with rheumatoid arthritis, has already been reported by Hardisty (1954).

Reviewing the literature since Lozner *et al.* (1940) first reported a case, Verstraete and Vandenbroucke (1956) were able to find 61 cases. Of these, 20 were in patients with haemophilia or Christmas disease who had developed the anticoagulant following blood transfusions; 16 were in women within one year of a pregnancy; one was in a newborn infant; eight were in females unrelated to pregnancy; and 16 in non-haemophiliac males. Most of the latter cases were associated with one or other of a variety of constitutional diseases, a list of which is given by Hougie (1955), but in a few no associated disease could be found (Joules and MacFarlane, 1938; Pons and de Torregrosa, 1952; Hougie, 1953; and others). The case reported here comes into the latter group.

Case History

A gardener aged 56 was sent into hospital by his doctor with a history of having spontaneously started passing blood-stained urine five weeks previously. At times it had been profuse, and small clots had been present. There was no frequency or dysuria. In the last two weeks he had also noticed the appearance of spontaneous bruising of his skin and had bled more readily after shaving. He also had palpitations on exercise and cramp-like substernal pain.

In the past he had had "black measles" during the 1914-1918 war and also nephritis, for which he was in hospital three months. He had never had any bleeding episodes or bruising previously. There was no family history of any bleeding disease.

On admission on April 8, 1955, he was very pale and slightly jaundiced. There were large bruises on both his arms. Petechiae were not seen in the skin. His pulse was 100 and blood pressure 120/70. A systolic murmur was present at the apex and there was slight oedema of the right ankle. Neither the liver nor the spleen was palpable, but the right kidney could be felt though it was not tender.

The urine on admission contained fresh blood, and microscopy showed red cells ++++ and occasional leucocytes. Culture grew *Escherichia coli*.

Cystoscopy revealed spurts of blood coming from the right ureteric orifice. Retrograde pyelography showed an irregular caliceal pattern on the right, with the ureter dilated and tortuous; it was supposed that this was due either to a new growth or to the presence of blood clots. Preliminary laboratory investigation showed: Hb 56% (8.3 g./100 ml.); red blood cells 2,990,000/c.mm.; C.I. 0.94; white cells 10,400 (neutrophils 79%, monocytes 10%, lymphocytes 1%); platelets 425,000/c.mm.; serum bilirubin 1.15 mg./100 ml.; blood urea 70 mg./100 ml. The blood group was A rhesus positive. It was noticed that the blood sent to the laboratory for grouping and cross-matching had not clotted after four hours, so further investigations were carried out.

Laboratory Investigations.—E.S.R. (Westergren) 62 mm. at first hour, 100 mm. at second hour. W.R. and Kahn tests were negative. Examination for cold agglutinins was negative. Agglutination against *Salmonella* and *Brucella* organisms was negative. Serum proteins 6.08 g./100 ml. (albumin 3.44 g., globulin 2.64 g.). A/G ratio 1.3:1. Electrophoresis of plasma showed a slight increase in the α_2 globulin, but was otherwise normal. Fibrinogen 650 mg./100 ml. Thymol turbidity and alkaline phosphatase were normal. Blood culture grew *E. coli* from the bile salt broth. The direct Coombs test was negative.

Investigation of Coagulation.—Clotting-time (Lee and White), 70 minutes. Prothrombin time, 15 seconds (control 15 seconds). Bleeding-time (Duke) normal. Clotting-time of recalcified plasma 430 seconds (control 160 seconds). Mixing-tests with patient's plasma and normal plasma showed that the patient's plasma, when mixed with normal plasma, had the power of prolonging the clotting-time of the latter (Table I). A modified prothrombin consumption test was abnormal.

TABLE I.—*Clotting-times of Mixture of a Normal and Patient's Plasma on Admission*

Source of Plasma	Quantities of Plasma (ml.) Used				
Patient	0·1	—	0·1	0·05	0·01
Normal	—	0·1	0·1	0·1	0·1
Saline	0·1	0·1	—	0·05	0·09
M/40 $CaCl_2$	0·2	0·2	0·2	0·2	0·2
Clotting-time in seconds	430	160	255	170	155

The results suggested the presence of a circulating anticoagulant in his blood, and on April 15 samples of plasma and serum were sent to Dr. W. R. Pitney, of the department of haematology, Postgraduate Medical School, Hammersmith, who kindly performed a thromboplastin generation

TABLE II.—*Results of Thromboplastin Generation Tests on Mixture of Patient's and a Normal Blood*

	Plasma	Serum	Platelets	1	2	3	4	5	6
A	Normal 0·2	Normal 0·2	Normal 0·2	60	19	10	10	10½	
B	Patient 0·2	,, 0·2	,, 0·2	70	60	60	60	45	45
C	Normal 0·1 Saline 0·1	,, 0·2	,, 0·2	28	13	13	12½	11	10½
D	Normal 0·1 Patient 0·1	,, 0·2	,, 0·2	60	40	26	23	22	22
E	Normal 0·2	Normal 0·1 Saline 0·1	,, 0·2	60	28	16	14	14	13½
F	,, 0·2	Normal 0·1 Patient 0·1	,, 0·2	37	15	11½	11	12	11½
G	,, 0·2	,, 0·2	,, 0·2	37	16	12	12	12	12½

test, the results of which are given in Table II, and on which Dr. Pitney commented as follows:

"These results showed a gross impairment of thromboplastin formation when the patient's $Al(OH)_2$ absorbed plasma mixture (B) is substituted for normal plasma mixture (A). An equal mixture of normal and patient's plasma showed defective generation, although normal plasma and saline mixture (C) was satisfactory. Probably there is some defect also in the patient's serum (12-second thromboplastin compared with normal of 10 seconds), but this was not evident on mixing-tests.

"Plasma thromboplastin was generated from normal plasma, serum, and platelets, and then the patient's plasma was added. This was unable to affect the potency of the thromboplastin formed, as judged by the speed of clotting of the normal high-spun plasma. The patient's plasma was clotted by normal plasma thromboplastin in the same time as normal plasma.

"These findings agree with the diagnosis of a circulating anticoagulant. The anticoagulant appears to be used up during coagulation. It is probable that the Christmas factor activity of the serum is normal. The anticoagulant is not effective against formed plasma thromboplastin and therefore is probably acting either against anti-haemophilic globulin (A.H.G.) or an intermediate product of thromboplastin formation."

A further sample of blood was kindly examined by Dr. Biggs, at Oxford, who confirmed the presence of an anticoagulant in the serum which inhibited the production of thromboplastin up to a dilution of 1:64.

Treatment and Progress

A transfusion of 3 pints (1½ litres) of group A rhesus-positive blood was given soon after admission, and this raised his Hb to 72%. Two weeks later a hard painful haematoma arose below the right buttock, and his Hb fell to 54%, so a further 2 pints (1 litre) of blood was given to which three ampoules of fibrinogen were added, after which he remained well and his Hb rose to 58%. On April 27 he was started on cortisone, 200 mg. a day, and this dose was gradually reduced to 25 mg. a day, as his general condition was good and no more haemorrhagic episodes had occurred. His haematuria had ceased on May 5 and never recurred again, but on May 22 a large painful haematoma arose in the deep tissues of the left calf and it was thought advisable to raise his cortisone to 200 mg. daily again. He remained well for the next three weeks and his cortisone was again gradually reduced to 50 mg. daily, but on June 16 another haemorrhage occurred into his left thigh and he was put back on to 200 mg. of cortisone daily. The next day he had extensive bruising of the chest wall, was pyrexial, felt ill, and his Hb had fallen to 42%.

Two pints (1 litre) of blood was transfused, and it was noticed that his ear bled all day from the prick done to estimate his Hb, and bruising had occurred where the drip was put up. These bruises and the haematoma gradually settled, and on July 4 he was reduced to 150 mg. of cortisone daily. Later in the month he had a haemarthrosis of his right knee and a large bruise developed on his back, but after this he was free for several weeks. He was discharged from hospital on August 31, still taking cortisone 100 mg. daily.

At no time during his stay in hospital did his Lee and White clotting-time fall below 40 minutes. The plasma clotting-times and mixing-tests were repeated but there was no improvement (Table III).

After discharge the patient was seen regularly at the out-patient department, and the cortisone was changed to prednisolone, the dose varying between 20 and 45 mg. daily, being adjusted to obtain a balance between his increase in weight if given too much and haemorrhagic episodes which seemed to occur if the dose was reduced too much. In spite of this he had repeated minor haemorrhagic episodes not severe enough to require hospitalization, and he was, of course, not allowed to resume his work as a gardener.

TABLE III.—*Clotting-time of Mixtures of a Normal and the Patient's Plasma 17 Months After First Admission*

	Quantity of Plasma in ml.					
Normal plasma	0·1	0·1	0·1	0·1	0·1	—
Patient's plasma						0·1
Patient's plasma diluted 1:2					0·1	
Patient's plasma diluted 1:5				0·1		
Patient's plasma diluted 1:10			0·1			
Patient's plasma diluted 1:100		0·1				
Normal saline ..	0·1					0·1
M/40 $CaCl_2$ ..	0·2	0·2	0·2	0·2	0·2	0·2
Clotting-time in seconds ..	126	160	182	215	235	330

This caused considerable social upset, as he had to give up his job and the cottage that went with it, and his wife had to go out to work.

He was readmitted for the first time in January, 1956, because of a large haematoma following venepuncture, and after this was comparatively well until his second admission in June, 1956, because of a large painful discharging swelling of his left elbow following a blister three days previously. He was found to have an abscess and cellulitis of his left arm, for which he was given oral oxytetracycline and his prednisolone was stopped. The abscess (which on culture grew *Staph. pyogenes*) had to be incised and drained surgically, and following this there was severe bleeding and he had to be given 3 pints (1½ litres) of blood.

He gradually improved and was discharged in the middle of July, 1956; he remained well without taking any prednisolone at all until November, when a large bruise developed on his left hand. Prednisolone, 15 mg. daily, was restarted, and, as further bruising appeared later in November, the dose was raised to 30 mg. daily.

The thromboplastin generation test was repeated and gave essentially similar results to the original test 18 months previously, both revealing the presence of a circulating anticoagulant in the plasma active at a dilution of 1 in 80.

A large haematoma of the right thigh sent him into hospital again in December, 1956, and his haemoglobin was then down to 56%, whereas it had been maintained at 90% during the previous months. In February, 1957, he developed a large haematoma of the left buttock, and in March a further haemorrhage into the left thigh for which he was admitted for the fourth and last time.

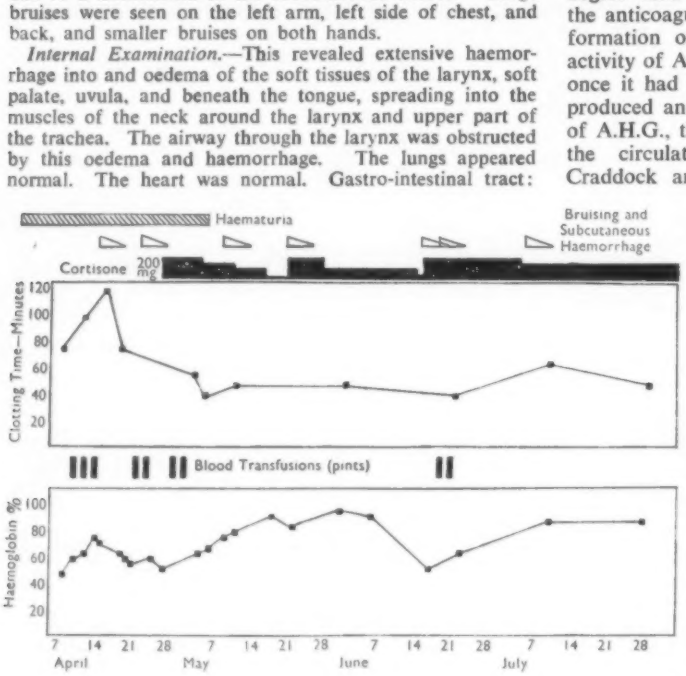
Whilst in hospital on March 22 he suddenly developed a large haemorrhage on the right side of the neck which spread under the tongue and into his throat, causing respiratory embarrassment, from which he finally died just two weeks short of two years since his first admission.

Post-mortem Findings

External Appearances.—The body was that of a middle-aged man of average nourishment. A large swelling due to a haematoma was present in the upper part of the chest and neck. There was swelling of the right side of the face

due to a haematoma in the subcutaneous tissues. Large bruises were seen on the left arm, left side of chest, and back, and smaller bruises on both hands.

Internal Examination.—This revealed extensive haemorrhage into and oedema of the soft tissues of the larynx, soft palate, uvula, and beneath the tongue, spreading into the muscles of the neck around the larynx and upper part of the trachea. The airway through the larynx was obstructed by this oedema and haemorrhage. The lungs appeared normal. The heart was normal. Gastro-intestinal tract: there were small haemorrhages on the peritoneal surfaces of the stomach but no bleeding into stomach or any other part of intestines. Liver and gall-bladder appeared normal. The kidneys were normal macroscopically, and the prostate was enlarged. The cortex of the adrenals was thin and of a bright yellow colour.



Histological examination of prostate, liver, and spleen disclosed no significant abnormality. The kidneys showed fibrosis of several glomeruli and focal lymphocytic infiltration only. The adrenals showed atrophy of the cortex, presumed to be due to prolonged cortisone therapy. No underlying organic disease could be found.

Discussion

An interesting feature of this case was the apparent reduction in frequency and severity of the haemorrhagic episodes during treatment with cortisone or prednisolone (see Chart) without any comparable improvement in the whole-blood clotting-time or the titre of the circulating anticoagulant.

Evans (1955) reported similar findings in one of his cases, and in the other case the clotting-time was reduced and the anticoagulant disappeared from the blood during treatment with cortisone; but these results may have been due to natural remission, as the titre of these anticoagulants has been shown to fluctuate spontaneously from time to time and even to disappear altogether (Soulier and Larrieu, 1953).

Most observers have failed to find any clinical or laboratory improvement when using cortisone (Frick, 1953, 1955; Hougie, 1953, 1955; Hougie and Fearnley, 1954; Verstraete and Vandenbroucke, 1956). Van Crefeld *et al.* (1953), however, reported a fall in activity of the anticoagulant following cortisone therapy, but the technique he employed to demonstrate this may give unreliable results (Hougie, 1955). They also found that, following corticotrophin or cortisone, the clotting-time could be reduced by plasma transfusions to a greater degree than before. As reported by previous authors, the anticoagulant in this case was shown to inhibit the formation of thromboplastin by interfering with the activity of A.H.G., but had no effect on thromboplastin once it had been formed. Richards and Spaet (1956) produced an antibody in rabbits by giving them doses of A.H.G., the properties of which were identical with the circulating anticoagulants found in humans. Craddock and Lawrence (1947) have also produced evidence that the anticoagulant appearing in haemophilic cases was an immune antibody and probably present in the gamma-globulin fraction of the serum or plasma.

Craddock and Lawrence were also able to demonstrate precipitins to A.H.G. in the serum of two cases, and several other workers have also obtained positive precipitin tests (Frommeyer *et al.*, 1950; Hougie and Fearnley, 1954; Verstraete and Vandenbroucke, 1956; and others). Collins and Ferriman (1952) suggested that the anticoagulant arising in non-haemophiliacs is an auto-antibody similar to that appearing in cases of acquired haemolytic anaemia, and Evans (1955) suggested that a response to cortisone in some of these cases could therefore be anticipated, considering the favourable response obtained sometimes in haemolytic anaemias. On the other hand, the apparent clinical improvement may be due to direct action on the capillaries similar to the symptomatic improvement seen in cases of thrombocytopenic purpura treated with cortisone, even when the platelet count remains low.

It is possible that the prednisolone precipitated the development of the cellulitis and abscess of the arm in this case, and the drug was withheld as soon as these developed.

However, until some more specific treatment becomes available it would seem well worth while giving prednisolone, as symptomatic improvement, at least, may result.

Summary

A case of haemorrhagic disease in a man aged 56, due to the presence of a circulating anticoagulant in his blood, is described.

The impression was gained that cortisone or prednisolone improved his clinical condition and reduced the frequency of his haemorrhagic episodes, although there was at no time any improvement in his whole-blood clotting-time or the titres of the anticoagulant. He survived for two years, eventually dying from asphyxia following haemorrhage into the larynx and base of the tongue.

No underlying organic disease could be found at necropsy.

I thank Mr. W. W. Gilford and Dr. R. M. Miller for permission to report one of their cases; Dr. W. R. Pitney for the thromboplastin generation tests and reports on them; and Mr. L. Rogers for the Chart.

REFERENCES

Collins, I. S., and Ferriman, D. G. (1952). *Lancet*, **2**, 712.
Craddock, C. G., jun., and Lawrence, J. S. (1947). *Blood*, **2**, 505.
Evans, D. M. D. (1955). *J. clin. Path.*, **8**, 168.
Frick, P. G. (1953). *Blood*, **8**, 598.
—— (1955). Ibid., **10**, 691.

Frommeyer, W. B., jun., Epstein, R. D., and Taylor, F. H. L. (1950). *Blood*, **5**, 401.
Hardisty, R. M. (1954). *J. clin. Path.*, **7**, 26.
Hougie, C. (1953). Ibid., **6**, 30.
—— (1955). *Brit. med. Bull.*, **11**, 16.
—— and Fearnley, M. E. (1954). *Acta haemat. (Basel)*, **12**, 1.
Joules, H., and MacFarlane, R. G. (1938). *Lancet*, **1**, 715.
Lozner, E. L., Jolliffe, L. S., and Taylor, F. H. L. (1940). *Amer. J. med. Sci.*, **199**, 318.
Pons, E. R., jun., and de Torregrosa, M. V. (1952). *Blood*, **7**, 20.
Richards, M. D., and Spaet, T. H. (1956). Ibid., **11**, 473.
Soulier, J. P., and Larrieu, M. J. (1953). *J. Lab. clin. Med.*, **41**, 849.
Van Crefeld, S., Hoorweg, P. G., and Paulssen, M. M. P. (1953). *Blood*, **8**, 125.
Verstraete, M., and Vandenbroucke, J. (1956). *J. Lab. clin. Med.*, **48**, 673.

CLINICAL METHOD OF ASSESSING TONUS AND VOLUNTARY MOVEMENT IN HEMIPLEGIA*

BY

J. BREWSTER BRENNAN, M.D., D.Phys.Med.
Department of Physical Medicine, St. James' Hospital, London

During the trial of a new method of spasmolysis in a series of hemiplegic patients difficulty was experienced in finding a method of clinical examination capable of providing an accurate record of the response to treatment. It was desirable to assess its effect upon both tonic spasm and voluntary movement, improvement in the latter being the ultimate aim. Some treatises, such as that by Kendall and Kendall (1949), give excellent guidance on examining individual muscles showing flaccid paresis, but no complete system of examining muscle groups presenting motor deficit and hypertonus has been found, though several workers have made valuable contributions (Teitelbaum and Vyner, 1949; Rinzler *et al.*, 1951; Twitchell, 1951; Hinckley, 1954).

Many difficulties and pitfalls are encountered in elaborating a satisfactory method. Foremost is the influence exerted by certain intrinsic and extrinsic factors upon the tonus and activity of spastic muscle. Among these are temperature, emotion, attitudinal reflexes, and synergy movement. A method of examination which aims to detect spontaneous change, or change in response to treatment, must have a rigid standardization of all such factors during each examination, otherwise the clinical findings may be quite misleading. When this has been done, some means of measuring change in the degree of tonus and in the range and power of voluntary movement is required. Electromyography or mechanical apparatus has usually been used (Berger and Schwartz, 1948; La Joie and Gersten, 1952; Basmajian and Szatmari, 1955), but it appears unsatisfactory that trials of new therapeutic agents of such increasing importance as the spasmolysants should be restricted to the few institutions where such instruments are available. Furthermore, neither apparatus is adequate for examining both of the above modalities.

The following clinical method was devised to study the hypertonic musculature of patients with residual hemiplegia, but it was also found applicable to most other upper motor neurone diseases. It is best described in two sections: the avoidance of errors which may arise through inadequate control of influencing factors and the method of examination. It is reported in the hope that it may provide a basis for further work.

*The work presented is part of the material submitted for the M.D. examination of Glasgow University.

Control of Factors Influencing Tonus and Activity in Skeletal Muscle

Temperature.—It is thought that external heat facilitates and that cold depresses voluntary muscle action (Schneider and Karpovich, 1948). Again, warming hypertonic muscle reduces the intensity of tonus and cooling increases it. Therefore, to avoid the influence of wide variations in temperature at different examinations all were conducted in a room which was comfortably warm—that is, between 70 and 80° F. (21 and 26.5° C.). More careful control of temperature does not appear to be required, since La Joie and Gersten (1952), studying the effect of heat on hypertonus, found that it was lessened only when the limb was thoroughly warmed by close-range heating.

Emotion.—Bucy (1949) noted that tonic muscle spasm was intensified by emotional stress. In my study it was found that excitement or worry could influence the examination findings to an appreciable extent. Certain steps were therefore taken to avoid strain. These were: exclusion from the examining room of all persons other than the patient and doctor; the patient was settled comfortably; examination was conducted quietly and methodically.

Attitudinal Reflexes.—Several workers have shown that these reflexes exert significant effects upon tone and movement in human hemiplegic patients (Yamshon, Machek, and Covalt, 1949; Twitchell, 1951; La Joie and Gersten, 1952). Their influence cannot be eliminated, but it can be standardized so that the findings are affected to equal degree at successive examinations. The following method was used: the upper limb was examined with the patient sitting upright and looking straight ahead at eye level; the lower limb was examined with the patient lying on the unaffected side, his head supported on a pillow so that it lay in line with the body. These positions were also convenient for conducting the examination.

Flexion and Extension Synergies.—If voluntary movement is not confined to the joint controlled by the muscle groups being tested the influence of synergy movements (Twitchell, 1951) may falsify the findings. The part of the limb (or body) proximal to the joint whose movement was being examined was therefore held immobile.

Volition.—It was observed that voluntary contraction of a hypertonic muscle group often led to a temporary increase in the tone of that group. Tonus was therefore assessed after active movement.

Rate of Passive Movement.—One of the methods used in estimating the intensity of tone was measuring the degree of resistance offered to passive movement. It has been noted (Twitchell, 1951) that the amount of resistance varies directly with the speed at which a hypertonic muscle group is stretched. An attempt was made to standardize this factor by moving the joint through its full range in the space of one second. It was not always possible to do so where hypertonus was pronounced, but only by attempting always to carry the movement through in that time could change in resistance be fairly assessed at different examinations.

Method of Examination

Tonus

Change in the intensity of tonus was measured in three ways, each of which was complementary to the others.

"*Range of Normal Tonus.*"—When any joint in an affected limb was moved passively from one extreme of its range to the opposite it was found that the early section of the total arc in either direction was free of resistance. In the series of residual hemiplegic patients studied the lengths of these arcs, under controlled conditions, remained constant in the absence of treatment. When, with spasmolytic therapy, tonus as measured by other means became less their lengths increased. This phenomenon was also noted by Teitelbaum and Vyner (1949) and Twitchell (1951). The length of the free arc was termed the "range of normal tonus" of the muscle group under observation, and its value was found to be a most reliable index of the degree of spasm. A goniometer was used to measure it.

Degree of Tonus.—In addition to measuring the range of normal tonus, the degree of resistance offered to passive movement through the remainder of the arc was measured. Symbols were used to record it: normal tonus=A, mild=B, moderate=C, marked=D, intense=E. Intermediate values were indicated by coupling letters. It was found that these values altered towards normality at the same time as the range of normal tonus increased. It may be worth recording that clasp-knife rigidity presented in only 70% of the muscle groups observed, the others offering a steady resistance throughout. In order to include both types of response in a standard method the degree of tonus was measured as the amount of resistance encountered in the first 10 to 15 degrees of the resisted arc.

Postural Position of Limb.—This method of measurement was applicable only to the upper limb. Before treatment began all patients held the arm adducted at the central and flexed at the peripheral joints. As tonus decreased a more normal resting posture was assumed. The angle of flexion at the elbow, wrist, and fingers became less acute and the amount of change compared with their original positions was recorded at each examination.

Voluntary Movement

Range.—The range of movement was measured with a goniometer.

Power.—The force of contraction was recorded in the manner recommended by the Medical Research Council. No movement=0, flicker of movement=1, movement with the force of gravity eliminated=2, movement against gravity=3, movement against gravity and resistance=4, normal power=5. Intermediate values were recorded by using the lesser figure followed by a plus sign. It was not uncommonly found that power varied in different sections of the arc through which active movement could be made. For example, a patient might be able to extend his elbow from the position of full flexion through an arc of 45 degrees with a power of 4+ but could only extend with a lessened force, perhaps 3+, through the remainder of the active range. Where such a feature could be measured a record of it was made. As might be expected, the locus at which this lessening of power became evident was usually close to that which marked the end of the "range of normal tonus."

Examination Procedure

To illustrate how the above system worked in practice the procedure for examining the flexors and extensors of the elbow joint are described. The patient was allowed to sit in a comfortably warm room for some 30 minutes before examination. Clothes above the waist were then removed, and he was seated on an upright chair and asked to look straight ahead. When he was comfortably settled and relaxed the angle of postural flexion at his elbow-joint was measured. Then, with the upper arm held still he was instructed to flex his elbow as far as possible and the range of flexion was measured. Next he extended it to the limit obtainable and the range of extension was noted. These movements were then repeated against resistance and the power gauged. Tonus was then measured, the examiner placing the elbow in the fully flexed position and attempting to put it through its full range of extension in the course of one second. This period of time was measured by saying the words "one million" *sotto voce*. When spoken deliberately they occupy one second. Within a few degrees of resistance becoming evident movement was stopped, the "range of normal flexor tonus" measured, and the degree of resistance recorded. This manœuvre was repeated three times to obtain an average figure. Tonus in the extensors was measured by reversing the procedure, beginning with the elbow in the fully extended position.

Summary

Examining hypertonic muscle groups presents difficulties which are not encountered in the examination of normal or flaccidly paralysed muscles. Chief of these is the influence upon the clinical findings of certain factors such as temperature, emotion, attitudinal reflexes, and synergy movements. Unless the effect of each of these is strictly and uniformly standardized the examination findings will not be a true reflection of change in tonus or active movement.

A method of clinical examination is described which is thought capable of providing accurate information regarding change, spontaneous or as a response to treatment, in the tonus and contractility of muscle groups presenting tonic spasm and motor deficit.

I thank Dr. P. Bauwens, physician-in-charge of the departments of physical medicine and electrodiagnosis, St. Thomas's Hospital, for his most helpful criticism of the work.

REFERENCES

Basmajian, J. V., and Szatmari, A. (1955). *A.M.A. Arch. Neurol. Psychiat.*, **73**, 224.
Berger, F. M., and Schwartz, R. P. (1948). *J. Amer. med. Ass.*, **137**, 772.
Bucy, P. C. (1949). *The Precentral Motor Cortex*, 2nd ed. Univ. of Illinois Press, Urbana.
Hinckley, K. F. (1954). *Phys. Ther. Rev.*, **34**, 520.
Kendall, H. O., and Kendall, F. P. (1949). *Muscles: Testing and Function*. Williams and Wilkins, Baltimore.
La Joie, W. J., and Gersten, J. W. (1952). *Arch. phys. Med.*, **33**, 595.
Rinzler, S. H., Brown, H., and Benton, J. G. (1951). *Amer. Heart J.*, **42**, 710.
Schneider, E. C., and Karpovich, P. V. (1948). *Physiology of Muscular Activity*, 3rd ed. Saunders, Philadelphia.
Teitelbaum, H. A., and Vyner, H. L. (1949). *Arch. Neurol. Psychiat. (Chicago)*, **62**, 92.
Twitchell, T. E. (1951). *Brain*, **74**, 443.
Yamshon, L. J., Machek, O., and Covalt, D. A. (1949). *Arch. phys. Med.*, **30**, 706.

Medical Memoranda

Argentaffin Tumour of the Ileum with Intussusception

According to Dangremond (1942), only 283 argentaffin tumours of the small intestine had been recorded in the literature since they were first recognized as a distinct entity by Oberndorfer (1907).

Ariel (1939), in a review of the cases published between 1930 and 1938, was able to record the age of the patients in 70 instances, and their disposition in decades was as follows :

0–10	..	..	Nil	31–40	..	..	6	61–70	..	..	17
11–20	..	..	Nil	41–50	..	..	9	71–80	..	..	9
21–30	..	..	1	51–60	..	..	27	81–90	..	..	1

He points out that the average age of 57.5 years differs greatly from that of the patients admitted to the Mount Sinai Hospital with appendicular tumours, whose average age was only 25. He attributes this to the much earlier onset of symptoms in the appendicular cases. This contrast had also been made by Humphreys (1934). Marfarlane (1957) has stated that in his own series of non-appendicular cases the extremes of age were 19 and 83.

The occurrence of one of these tumours in the ileum in a boy of 4 years is therefore of considerable interest. It has long been known that these tumours grow extremely slowly, and according to Cope (1930) may attain a large size and then remain stationary for years. Many cases may therefore originate in infancy or childhood, and we believe our case to be the first to confirm what has previously been a speculation.

CASE HISTORY

A boy of 4 years was admitted to hospital on September 22, 1957, with a three-days history of generalized abdominal pain, diarrhoea, and repeated vomiting. He was flushed, his tongue was coated, and his abdomen was soft and distended. Rectal examination showed the presence of watery altered blood, and *x*-ray examination showed gaseous distension of the small gut and a fluid level in the stomach.

Operation.—At laparotomy an ileo-colic intussusception was found. This was reducible except for the last 4 in. (10 cm.) of the ileo-ileal segment. This portion was resected and an end-to-end anastomosis carried out. Recovery was uneventful.

Pathology.—The resected intussusception was firmly fixed and irreducible. At its apex there was a firm white submucous nodule 1 cm. in diameter. The gut was purple from the extravasated blood and the mucosa was coated by fibrinous exudate. Histological sections showed the tumour lying between the muscle coat and the degenerating mucosa. It was composed of islands of solidly packed anaplastic cells with no structural arrangement and separated by a delicate fibrous stroma. There was no capsule. In sections stained by Levaditi's method the cells were seen to be packed by grey-brown silver-retaining granules.

COMMENT

These tumours come to light in six different ways: (1) As unexpected findings at necropsy. Dangremond's series of 46 included 23 found this way. All the six recorded by Willis (1940) were necropsy cases, as were the nine described by Raiford (1933). At least half the published cases appear to have been " pathologist cases " and had presumably been symptomless. (2) In the operative treatment of acute or subacute obstruction. No fewer than 33 of Ariel's 79 review cases fall into this category. This is the usual clinical manifestation. (3) A large tumour may undergo a central necrosis and lead to perforation. This is rare, but cases have been described by Cooke (1931) and Stewart and Thomson (1951). (4) A nodular growth may lead to intussusception as in our case. In Ariel's review series it was seen once in a man of 52, and among the 11 cases in Ariel's personal series there was one instance in a man of 32. This complication is unlikely once the tumour has reached a certain size because of its diffusive infiltration of the mucosa and the muscle. (5) The discovery of a painless mass in the abdomen during life. (6) If the tumour, together with its metastases, is bulky enough the secretion of 5-hydroxytryptamine may lead to the clinical syndrome of flushing, with cyanosis, diarrhoea, and other symptoms described by Biörck and his colleagues (1952).

Consideration of these six groups makes it evident that in a child of 4 years, apart from the improbable event of a small nodule being found at necropsy, by far the most likely way for the tumour to come to light would be in relation to an intussusception. From this it follows that the apex of any intussusception in a child should be rigorously searched. In our case, had the surgeon not drawn attention to what appeared to be a scar in the region of the tumour the pathologist would almost certainly have overlooked it. The swollen, distorted, and discoloured gut will of course obscure small submucosal tumours.

The presence of other neoplastic centres or of metastases cannot be ruled out. According to Macfarlane the value of estimating 5-hydroxyindole acetic acid (the end-product of 5-hydroxytryptamine) in the urine, after surgical removal of a tumour, in terms of its ability to indicate early metastases, has not yet been established. The urine in our case was examined a month after the operation and no significant rise found. Logically the patient should be brought to hospital for the urine to be examined every year or so, but the psychological damage which might result in the future should be carefully weighed before a lifelong observation is undertaken.

We are indebted to Mr. Kenneth Aulton for the chemical examinations.

E. T. MCCARTNEY, *M.C.*, M.B., F.R.C.S.,
I. STEWART, M.D.,
Victoria Hospital, Keighley.

REFERENCES

Ariel, I. M. (1939). *Arch. Path. (Chicago)*, **27**, 25.
Biörck, G., Axén, O., and Thorson, A. (1952). *Amer. Heart J.*, **44**, 143.
Cooke, H. H. (1931). *Arch. Surg. (Chicago)*, **22**, 568.
Cope, Z. (1930). *Brit. J. Urol.*, **2**, 268.
Dangremond, G (1942). *Amer. J. clin. Path.*, **12**, 223.
Humphreys, E. M. (1934). *Amer. J. Cancer*, **22**, 765.
Macfarlane, P. S. (1957). *Proc. roy. Soc. Med.*, **50**, 443.
Oberndorfer, S. (1907). *Frankfurt. Z. Path.*, **1**, 426.
Raiford, T. S. (1933). *Amer. J. Cancer*, **18**, 803.
Stewart, I. S., and Thomson, G. R. (1951). *Brit. med. J.*, **2**, 1316.
Willis, R. A. (1940). *Med. J. Aust.*, **2**, 400.

Reviews

HARVEY ON THE CIRCULATION

The Circulation of the Blood. Two Anatomical Essays by William Harvey, together with Nine Letters written by him. Translated from the Latin and slightly annotated by Kenneth J. Franklin. (Pp. 184; illustrated. 22s. 6d.) Oxford: Blackwell Scientific Publications. 1958.

Professor K. J. Franklin has followed up his translation of *De Motu Cordis*, which was published in 1957, with an equally excellent one of *De Circulatione Sanguinis*, as Harvey's two anatomical essays, addressed in 1649 to Jean Riolan, jnr., are commonly called. These essays are significant as giving Harvey's mature reflections on the circulation of the blood. They show the courteous and convincing manner in which he replied to his critics and opponents, and his further application of the experimental method in his researches and in the teaching of medical students. The nine letters relate also to Harvey's scientific and medical investigations, which he continued almost to the end of his life. The first letter, to Caspar Hoffmann (1572–1648), Professor of Medicine in Altdorf, Switzerland, is written on 20 May, 1636, by Harvey from Nuremberg, when he accompanied the Earl of Arundel's Embassy. Hoffmann denied the greater circulation, and Harvey offers to demonstrate his discovery anatomically and to attend on Hoffmann whenever he wishes. Tradition says the demonstration was made, but Hoffmann remained unconvinced, whereupon Harvey flung down his scalpel and stormed out of the dissecting-room.

The publication of *De Motu Cordis* in 1628 made no great stir in the medical world of that day. In England and Holland truth gradually made headway, especially in the College of Physicians and in the universities. In France, except for Descartes, the reception of Harvey's discovery was chiefly sceptical. The most serious opponent was Riolan: "John Riolan, the Son, the most experienced physician in the universitie of Paris, the Prince of Dissection of Bodies, and the King's professor and Dean of Anatomie and of the knowledge of simples, chief-physician to the queen-mother of Louis XIII," as Harvey describes him. In the *Encheiridium Anatomicum et Pathologicum*, 1648, a copy of which was sent to Harvey, Riolan restricted his belief in the circulation to certain parts of the body and clung to the old idea that blood passed through the septum of the heart. In the following year he expanded his views in his *Opuscula Anatomica Nova*. In these essays to Riolan Harvey maintained the existence of the circulation of the blood and supplied additional experimental evidence of its truth. He erred in assuming that the blood was deprived of "heat" and "vital spirit" on leaving the organs of the body. As Dr. Chauvois has pointed out, the re-examination of the Latin text of these essays shows that some current explanations of Harvey's teaching on the circulation are erroneous, especially as to the heart being its initiator. The essays to Riolan with the nine letters constitute a remarkable and essential addition to *De Motu Cordis*.

Physiology and medical history are once again indebted to Professor Franklin, who includes the Latin text with his English version. The publishers deserve praise for the book's good printing and presentation, including the coloured frontispiece representing the princes Charles and James at the Battle of Edgehill, 1642, where Harvey was in charge of them. This reproduction is the gift of Mr. Dickson Wright, the inspiring President of the Harvey Tercentenary Congress of 1957. It is from the oil-painting by William Dobson, presented by King Charles I to William Harvey, which now hangs in the Scottish National Portrait Gallery, Edinburgh.

ARTHUR S. MACNALTY.

DRUG SENSITIVITY

Sensitivity Reactions to Drugs. A Symposium Organized by the Council for International Organizations of Medical Sciences. Edited by M. L. Rosenheim and R. Moulton. (Pp. 237+x; illustrated. 35s.) Oxford: Blackwell Scientific Publications. 1958.

International organizations are increasing. Under the joint auspices of Unesco and W.H.O. there exists the Council for International Organizations of Medical Sciences. Last year the International Society of Clinical Pathology suggested to the Council that a symposium should be held on "Sensitivity Reactions to Drugs," and this book is an account of it. The symposium was held in Liège, and, probably because there were only 24 people there, it seems to have been very successful. Some 18 papers were presented, which for the most part were admirably brief, and, now that they are published, of great interest to those unacquainted with the evidence. For example, most people are aware that various substances (among which are promin, phenylsemicarbazide, primaquine, stibophen, and quinine) sometimes cause haemolysis, but probably few know that the anticonvulsant drugs phenytoin, primidone, and phenobarbitone occasionally give rise to megaloblastic anaemia. When they do the situation can be greatly improved by giving folic acid. Valuable papers were contributed by L. P. Garrod (one on the production of bone-marrow aplasia by chloramphenicol and the other on sensitivity reactions to antibiotics); also by B. N. Halpern on the antibodies produced in drug allergy, which he showed could be transmitted to other subjects; and by A. R. Rich on the tissue reactions produced by sensitivity to drugs. A simple account of those medicinal substances which cause release of histamine in the absence of previous sensitization was given by J. Lecomte. There were several other contributions.

The book containing these papers has been edited very successfully by Professor M. L. Rosenheim and Dr. R. Moulton, so that it is concise, informative, and readable. It is a most useful volume.

J. H. BURN.

ESSENTIALS OF CARDIOLOGY

Basic Cardiology. By T. E. Gumpert, M.B., Ch.B.(Sheff.), F.R.C.P.(Lond.). (Pp. 168+viii; illustrated. 25s.) Bristol: John Wright and Sons, Ltd. 1958.

In this short volume which embraces the essentials of cardiology Dr. T. E. Gumpert has brought together a number of lectures delivered to students. A compilation of this kind ensures that a reasoned explanation is given of the main clinical problems of cardiology; at the same time, the frequent emergence of a colloquial style, as in the examples of clinical cases, stimulates the reader's interest and critical faculty. The fact that the book contains only 160 pages means that there has been much compression of the material, and in achieving this the author has made an excellent choice in order to maintain balance. Some over-simplification has been inevitable, but for undergraduate students this is not disadvantageous. Dr. Gumpert has given much expert

advice regarding treatment, and this aspect of cardiology is well handled and up to date—for example, the use of radioactive iodine, current usages in the treatment of bacterial endocarditis, and the administration of anti-coagulants. Any student wishing for clearly explained and brief accounts of the principles of modern cardiology could not do better than study the chapters of this book.

K. SHIRLEY SMITH.

TRAPS FOR THE SURGEON

Fehler und Gefahren bei Chirurgischen Operationen. 4th edition. Edited by R. R. Stich and K. H. Bauer. 2 volumes. (Pp. 1,646; illustrated. DM. 76.50.) Jena: Gustav Fischer Verlag.

"Mistakes and Dangers in Surgical Operations" is the somewhat misleading title of a great work which represents German surgery at its highest level. More than 20 surgeons of wide experience have contributed full accounts of their varied fields of work, of the difficulties with which they have met, and of the precautions which they take to avoid them. It is impossible in a review to give any idea of the vast amount of detail of vital importance here collected, but perhaps two examples will serve to show its character. The risk of nerve injury in operations on the thyroid is well known, but we venture to think that few surgeons can be familiar with the many possibilities of injury which are here illustrated from precise dissections specially made with this object, whilst avoidance of the parathyroids is very clearly demonstrated. Gall-stones and the bile ducts present unlimited traps for the unwary, and here again we find every conceivable variation both of the ducts and of the arteries described and illustrated, whilst all the most modern methods of diagnosis in this difficult region are fully detailed.

In every article throughout the work we find the same complete discussion of the particular problems involved, of how they may be met, and of the peculiar difficulties which may arise. The value of such experience so clearly and candidly expressed is unlimited. Moreover, each section has a vast bibliography for those who wish to trace the sources of the methods and views described. The whole work impresses one by its thoroughness, and is indeed a splendid tribute to the surgery of Germany and Switzerland. We can only say that any surgeon who masters what he will find here about his own section—and no one could do more—far from making mistakes and meeting with dangers, will be well on the way to certainty and success.

HENRY SOUTTAR.

TUMOUR SURGERY

Tumor Surgery of the Head and Neck. By Robert S. Pollack, M.D., F.A.C.S. (Pp. 101; illustrated. 37s. 6d.) London: Henry Kimpton. 1957.

This is a modest book of some 100 pages with perhaps a slightly misleading title. It is concerned for the most part with the surgical techniques for extirpating malignant tumours of the paranasal sinuses, mouth, larynx, and pharynx, and of the thyroid gland. Due emphasis is given to the importance of accurate diagnosis and assessment of the extent of the lesion, and the relative roles of surgery and of radiotherapy are discussed. Operations are described briefly but adequately, and the illustrations are clear. It is not expensive—by current standards—and should be useful to those surgeons who have to deal with these lesions.

D. W. C. NORTHFIELD.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The Free Family. A Creative Experiment in Self-Regulation for Children. By Jean and Paul Ritter. (Pp. 269; illustrated. 18s.) London: Victor Gollancz Ltd. 1959.

Herdinfektion und Allergische Erkrankungen. Edited by H. Redetzky and H. Thiele. (Pp. 268; illustrated. DM. 17.) Berlin: VEB Verlag Volk und Gesundheit. 1958.

Directory of Social and Health Agencies of New York City, 1958-1959. Prepared under the direction of the Committee on Information Services of the Community Council of Greater New York, Inc. (Pp. 640+xi. 60s.) New York: Columbia University Press. London: Oxford University Press. 1958.

Psychopathologie Générale. By Gabriel Deshaies. (Pp. 211. 700 fr.) Paris: Presses Universitaires de France. 1959.

Safe Handling of Radio-isotopes. (Pp. 99. 6s.) Vienna: International Atomic Energy Agency. 1958.

The Pathology and Management of Portal Hypertension. By R. Milnes Walker, M.S., F.R.C.S. (Pp. 113+vii; illustrated. 35s). London: Edward Arnold (Publishers) Ltd. 1959.

Modern Trends in Diseases of the Vertebral Column. Edited by Reginald Nassim, B.M., F.R.C.P., and H. Jackson Burrows, M.D., F.R.C.S., F.R.A.C.S. (Pp. 292+ix+11; illustrated. 75s.) London: Butterworth and Co. (Publishers) Ltd. 1959.

Chronische Hyperplasien der Bindehaut. By Konstantin Pascheff. (Pp. 124; illustrated. DM. 25.65.) Halle (Saale): VEB Carl Marhold Verlag. 1959.

Klinische Untersuchungen zur Frage der Ätiologie des primären Glaukoms. By Professor G. Pietruschka, M.D. (Pp. 295. DM. 36.80.) Halle (Saale): VEB Carl Marhold Verlag. 1959.

Medical Laboratory Investigations. Their Use and Interpretation. By Ian Dawson, M.A., M.D., M.R.C.P., and William Goldie, M.A., M.B., F.R.C.P., F.R.C.P.(E.). (Pp. 260+xv; illustrated. 35s.) London: Butterworth and Co. (Publishers) Ltd. 1958.

Anatomy for Surgeons. Vol. 3. The Back and Limbs. By W. Henry Hollinshead, Ph.D. (Pp. 901+xii; illustrated. £8 8s.) London: Cassell and Company Ltd. 1959.

Pulmonary Circulation. An International Symposium, 1958. Sponsored by the Chicago Heart Association. Edited by Wright R. Adams, M.D., and Ilza Veith, Ph.D. (Pp. 316+xv; illustrated. $4.50.) New York, London: Grune and Stratton. 1959.

Die Grundlagen der Eierschalentherapie. By Professor Stefan Krompecher, M.D. (Pp. 83+ix; illustrated. DM. 11.) Jena: VEB Gustav Fischer Verlag. 1958.

Entstehung und Verhütung von Lebensmittelvergiftungen durch Salmonellabakterien. By Dr. Hans Dräger. (Pp. 98+v. DM. 5.60.) Jena: VEB Gustav Fischer Verlag. 1958.

Treatment of Lung Cavities and Endobronchial Tuberculosis. With Special Reference to Treatment in Malaya. By Beryl E. Barsby, M.D., M.R.C.P. (Pp. 147+vi; illustrated. 20s.) Edinburgh and London: E. and S. Livingstone Ltd. 1959.

First Afro-Asian Congress of Ophthalmology, 1-5 March, 1958. Cairo, United Arab Republic. Acta. (Pp. 734 + lxxii; illustrated.) Cairo: Ophthalmological Society of Egypt. 1958.

A Doua Consfatuire de Dermato-Venerologie pe Tara, Iasi, 25, 26 si 27 Octombrie 1957. (Pp. 410; illustrated.) Bucharest: Editura Medicăla. 1958.

Rachitismo, Malattia Sociale. By Professor Emilia Sorrentini. (Pp. 53.) Rome: Istituto di Medicina Sociale. 1958.

L'Ulcera Gastro-Duodenale. Aspetti Clinici e Patogenetici di Patologia Geografica. By E. Pisi and L. Barbara. (Pp. 332+xi.) Bologna: Casa Editrice Cappelli. 1958.

Parasitology and Parasitologists in Poland. A General Review of Progress in Parasitological Science in Poland, containing Lists of Institutions, Research Workers and the Problems. By Professor Dr. E. Grabda, Dr. Z. Kozar and Dr. W. Slusarski. (Pp. 118.) Warsaw: Polish Parasitological Society. 1958.

Die Phenothiazinderivate in der Medizin. Klinik und Experiment. Edited by Professor H. Kleinsorge, M.D., and Dr. K. Rösner. (Pp. 328; illustrated. DM. 31.60.) Jena: VEB Gustav Fischer Verlag. 1958.

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THE ARTIFICIAL KIDNEY

Dialysis by an artificial kidney is sometimes required in the management of patients suffering from renal failure with oliguria. Until an adequate spontaneous diuresis occurs, the nitrogenous and mineral products of protein metabolism, which are normally excreted in the urine, accumulate in the body; and this process, if not prevented, will lead to death. J. J. Abel and colleagues[1] first suggested the term artificial kidney and were able to effect dialysis by passing animal blood treated with hirudin (the anticoagulant obtained from leeches) through collodion tubing immersed in fluid. The successful clinical application of this technique had to await the coming of heparin and suitable plastic tubing, so that thirty years elapsed before W. J. Kolff and H. T. J. Berk[2] described their prototype machine, which was built and used in Holland during the German occupation of that country.

Several different machines[3-9] have since been described, but, broadly speaking, there are only two types—the ultra-filtration kidney and the rotating-coil kidney. All, however, depend on the basic fact that "cellophane" membrane, properly prepared, allows diffusible molecules to pass its pores. When cellophane is interposed between the blood of a uraemic patient and a specially prepared fluid medium (the ionic contents and concentration of which approximate to those of the extracellular fluid of a normal subject) controlled exchanges are possible: urea, creatinine, uric acid, sodium, calcium, potassium, magnesium, chloride, bicarbonate, sulphate, phosphate, and water readily traverse the pores of the membrane, whereas large molecules, such as those of protein, will not pass.

In the Skeggs–Leonards ultra-filtration artificial kidney[5] a high-pressure system is used to circulate the patient's blood through an arrangement of multiple, paired, short, broad sheets of cellophane, which are placed between firm rubber pads. The blood is pumped in one direction while the dialysing fluid flows in the opposite direction along grooves in the rubber pads. In the ultra-filtration machine devised by Aoyama and Kolff[9] a similar high-pressure system is used to circulate the patient's blood through two parallel, long, narrow coils of cellophane tubing which are attached to and supported by a vertical mesh screen housed in a metal container. The dialysing fluid flows in at the bottom of the container and overflows freely at the top. Since the effective circulating blood pressure of these ultra-filtration machines is greater than the hydrostatic pressure of the fluid medium which surrounds the cellophane, water is transferred from the circulating blood into the dialysing fluid: between 700 and 1,000 ml. of water per hour may be removed from patients in this way.

The rotating-coil artificial kidney employed by Drs. F. M. Parsons and B. H. McCracken, the design and clinical use of which they describe in an article in this week's *Journal*, is a modification of the original machine described by Kolff. In this apparatus the patient's blood is circulated at a relatively low pressure through a long length of narrow cellophane tubing which is spirally wound round a horizontally rotating wire-mesh drum half-immersed in a metal tank of dialysing fluid. Transference of water is influenced by adjustment of the osmotic pressure gradient between the circulating blood and the dialysing fluid. Parsons and McCracken use a concentration of dextrose of 400 mg. per 100 ml. in the tank fluid for this purpose, but others prefer a higher concentration.

The artificial kidney may be used for the removal of poisons such as barbiturates, bromides, and salicylates, and at p. 752 of the *Journal* this week Drs. K. D. G. Edwards and H. M. Whyte describe a development of this idea. They studied patients with defective renal function who required streptomycin for treatment of infection. In order to reduce the risk of vestibular damage Edwards and Whyte successfully used an artificial kidney to hasten removal of streptomycin from the blood stream in five cases. But the artificial kidney finds its chief use in the treatment of patients with oliguric renal failure. A favourable outcome may be expected when the patient can recover from the renal lesion, as in cases of acute tubular necrosis and acute nephritis. But, as

[1] Abel, J. J., Rowntree, L. G., and Turner, B. B., *J. Pharmacol. exp. Ther.*, 1914, **5**, 275.
[2] Kolff, W. J., and Berk, H. T. J., *Acta med. scand.*, 1944, **117**, 121.
[3] Alwall, N., ibid., 1947, **128**, 317.
[4] Murray, G., Delorme, E., and Thomas, N., *Arch. Surg. (Chicago)*, 1947, **55**, 505.
[5] Skeggs, L. T., Jr., Leonards, J. R., and Heisler, C. R., *Proc. Soc. exp. Biol. (N.Y.)*, 1949, **72**, 539.
[6] Merrill, J. P., Thorn, G. W., Walter, C. W., Callahan, E. J., and Smith, L. H., *J. clin. Invest.*, 1950, **29**, 412.
[7] Rosenak, S. S., and Saltzman, A., *Proc. Soc. exp. Biol. (N.Y.)*, 1951, **76**, 471.
[8] MacNeil, A. E., *United States Army Medical Research Progress Report*, 1954, p. 502.
[9] Aoyama, S., and Kolff, W. J., *Amer. J. Med.*, 1957, **23**, 565.
[10] Bull, G. M., Jockes, A. M., and Lowe, K. G., *Lancet*, 1949, **2**, 229.
[11] Shackman, R., *Brit. J. Urol.*, 1958, **30**, 473.
[12] Brun, C., and Raaschou, F., *Arch. intern. Med.*, 1958, **102**, 716.

Parsons and McCracken have shown, some patients with renal failure require dialysis as a life-saving measure before it is realized that renal restitution can never take place : complete cortical necrosis, chronic pyelonephritis, thrombosis of renal vein, and amyloid disease are examples. Furthermore, a primary extra-renal lesion, itself responsible for the development of renal failure, may cause death despite dialysis and biochemical improvement—as in peritonitis, staphylococcal pneumonia, and severe multiple injuries. Overall mortality figures for dialysis by the artificial kidney therefore need to be interpreted with care, and the incidence of irreversible renal and fatal extrarenal lesions should be taken into account when assessing the value of the technique. On the other hand, many patients with oliguric acute renal failure recover with conservative treatment alone[10] and do not require dialysis. If all such patients were treated by the artificial kidney and success was attributed to the machine there would be an impressive incidence of success. Parsons and McCracken report that 82% of their patients required dialysis, but a significantly smaller figure has been quoted by others.[11]

There are no absolute indications for dialysis except a level of serum potassium which, despite treatment with ion-exchange resins, intravenous dextrose with insulin and calcium, and sodium lactate, produces electrocardiographic abnormalities, but many workers would agree with the biochemical and clinical criteria suggested by Parsons and McCracken. Renal biopsy may have a place in the management of those patients in whom an irreversible renal lesion is suspected ; C. Brun and F. Raaschon[12] have recorded some experience of this aspect of the problem.

Special units are required to operate the artificial kidney, but it is doubtful whether there is a need for more than about six such units in the whole of Great Britain and Northern Ireland. The units would need to be properly sited, and due regard should be paid not only to population and geography but also to the ready availability of a practised team. The technique itself requires a specially trained nurse, a biochemist, and two medical men, but, more important, expert medical, surgical, gynaecological, cardiological, haematological, and radiological opinion may be required at short notice. Finally, experience has shown that uraemic patients are particularly prone to acquire hospital infection. Therefore dialysis is best carried out in the equivalent of an operating-theatre, and cubicle accommodation with adequate facilities—including a sufficiency of nurses—is needed for the proper care of patients before and after such treatment.

POST-TRAUMATIC GIDDINESS

The complaint of dizziness or giddiness is common in patients who have had a head injury. Before an accurate diagnosis can be made or effective treatment be given, one must obtain as good a description as possible of the patient's subjective sensations, for the terms used may describe a large variety of unpleasant feelings. Some patients refer to a feeling of faintness, due to vasomotor instability, which is not uncommon after a severe head injury or indeed in the convalescent period after any severe illness or operation, while others may with the same words describe the sensations of anxiety, unsteadiness, and lack of confidence which are so common in post-traumatic neuroses. In a case of severe closed head injury there may be damage to the brain-stem and cerebellar connexions, and in such patients as a sequel of the injury there may be ataxia in walking and at times episodes of vertigo " in which the senses are deceived into seeing or feeling movement."[1] In cases of this type objective neurological signs of damage to the brain-stem will frequently be present. Post-traumatic epilepsy may occasionally be preceded by a feeling of giddiness, especially when the site of origin of the attack is in a temporal lobe, but then the giddiness is followed by impairment of consciousness, sometimes of very short duration. An electroencephalographic recording may be of help in the diagnosis, but a lack of epileptic patterns in a record made between seizures does not rule out the diagnosis of epilepsy. In such cases treatment with anticonvulsants is worth giving.

In many cases of post-traumatic vertigo the lesion is in the inner ear rather than in the central nervous system. When there has been a fracture in the temporal bone (and this is sometimes difficult to demonstrate radiologically), there may be damage to both the cochlea and the vestibular apparatus, and the patient may experience, in addition to perception deafness and tinnitus, paroxysmal attacks of severe vertigo with vomiting which are clinically similar to those which occur in Ménière's disease. N. Gordon[2] and Spencer Harrison[3] have drawn attention to another form of post-traumatic vertigo which is not rare. In this type vertigo occurs on sudden movements of the head—for example, in looking up at an aeroplane or hanging the washing out on a clothes line —and also frequently when the patient lies down or turns over in bed or gets up quickly in the morning.

[1] Cawthorne, T., *Brit. med. J.*, 1952, **2**, 931.
[2] Gordon, N., *Lancet*, 1954, **1**, 1216.
[3] Harrison, M. S., *Brain*, 1956, **79**, 474.
[4] Dix, M. R., and Hallpike, C. S., *Proc. roy. Soc. Med.*, 1952, **45**, 341.
[5] Pratt, R. T. C., and McKenzie, W., *Lancet*, 1958, **2**, 347.
[6] Havinga, H., *Ned. milit. geneesk. T.*, 1958, **11**, 187.
[7] Gillhespy, R. O., and Ratcliffe, A. H., *Brit. med. J.*, 1955, **2**, 352.

These patients suffer rotational vertigo lasting from a few seconds up to a minute or so, occasionally severe enough to make them fall. Deafness, tinnitus, and abnormal neurological signs are usually absent, and the caloric tests are frequently normal. An attack can often be precipitated by correct positioning of the patient, and this is helpful in confirming the diagnosis. The patient should sit on a couch with his head to one side, and his head should then be rather quickly lowered over the end of the couch, when vertigo and nystagmus will occur either immediately or after a delay of a few seconds. The vertigo and nystagmus usually cease within a minute or so, but may occur transiently when the patient sits up. If the test is repeated immediately, the response is considerably less than on the first occasion, and it may not occur again with similar positioning for some time. If the characteristic response does not occur in a suspicious case with the head turned to one side, the manœuvre should be repeated with the head turned to the opposite side. This is the condition which M. R. Dix and C. S. Hallpike[4] have described as positional nystagmus of the benign paroxysmal type, and it may occur in patients who have not had a head injury. It is thought to be due to an irritative lesion in the otolith system. Spencer Harrison, in studying 104 patients suffering from this condition, noted that nineteen had a preceding head injury which he considered to be the precipitating factor.

It is clearly important to recognize this disorder not only in cases of head injury but also when it arises spontaneously. It has long been known that sufferers from vertigo may develop severe anxiety or hysterical symptoms, and unless the history is carefully taken it is easy to overlook the organic factor in vertigo and ascribe the whole condition to psychogenic factors, as R. T. C. Pratt and W. McKenzie[5] have recently emphasized, with resultant failure in treatment and of the patient's confidence in the doctor. Post-traumatic positional vertigo of this type usually improves gradually over the course of months, but may persist for considerably longer. Sufferers can learn to avoid the type of movement which precipitates giddiness, and the disorder is often helped by administration of dimenhydrinate, promethazine, or cyclizine. H. Havinga[6] has recently reported that orphenadrine has been effective in the treatment of post-traumatic giddiness; he describes five patients, and though the clinical account is not detailed the description suggests that they were suffering from positional vertigo of peripheral origin. This drug, which has proved useful in the symptomatic treatment of Parkinsonism,[7] has a mild antihistamine and a marked anticholinergic action and would seem worth further trial in post-traumatic and "spontaneous" positional vertigo.

MALIGNANT CELLS IN THE BLOOD STREAM

Though the haematogenous spread of malignant disease has been observed for many years, the detection of cancer cells in the peripheral blood stream has been difficult. Probably T. R. Ashworth[1] was the first to recognize such cells, and he reported his observations in the *Australian Medical Journal* as long ago as 1869. The case was one of multiple malignant skin tumours, and he found that the blood after death contained cells similar to those in the tumours. Many other workers have confirmed this work. In 1903 M. B. Schmidt[2] examined the lungs of 41 patients dying of cancer but without visible pulmonary metastases and found emboli of malignant cells embedded in fibrous tissue. He concluded that the majority of such cells perished or at least were incarcerated.

Over the years much experimental work on the production of metastases in animals has been done, but it was not until 1955 that H. C. Engell,[3] of Copenhagen, reported in a classic paper a large number of cases investigated during operations for excision of tumours. In 76 cases of rectal cancer he found malignant cells in the venous drainage of 41; similarly in 31 cases of colonic cancer he found malignant cells in 22. Thus, of 107 cases, 59% were positive. Follow-up showed that such cells were found equally in patients whose disease recurred from six months to four years as in those who survived for more than four years. His conclusions were: firstly, that haematogenous spread depends on the grade of differentiation of the tumour; secondly, the demonstration of cells is made too seldom to be of diagnostic significance; thirdly, no prognostic importance should be derived from the presence of cells; and, fourthly, there was no proof that manipulation of the tumour during operation led to an increase in the escape of tumour cells. From the last it followed that even ligature of all veins before mobilization of the tumour would be unlikely to reduce the incidence of haematogenous metastases.

Since 1955 Warren Cole and his associates in Chicago have published a series of clinical and experimental papers on the problem.[4-7] Using the Walker carcinosarcoma 256 of rats they have shown that, the more cancer cells injected, the greater the number of metastatic "takes." Injection of nitrogen mustard (HN2) into the portal vein, a systemic vein, or intraperitoneally at the same time significantly reduced the

[1] Ashworth, T. R., *Aust. med. J.*, 1869, **14**, 146.
[2] Schmidt, M. B., quoted by H. C. Engell in *Acta chir. scand.*, 1955, Suppl. 201.
[3] Engell, H. C., ibid., 1955, Suppl. 201.
[4] Cole, W. H., Cruz, E. P., and McDonald, G. O., *Surgery*, 1956, **40**, 291.
[5] —— McDonald, G. O., Livingston, C., and Boyles, C. F., *Ann. Surg.*, 1957, **145**, 624.
[6] —— Morales, F., Bell, M., and McDonald, G. O., ibid., 1957, **146**, 588.
[7] —— Economou, S. G., Mrazek, R., McDonald, G. O., and Slaughter, D., *Ann. N.Y. Acad. Sci.*, 1958, **68**, 1097.
[8] Shapiro, D. M., and Fagmann, R. A., *Cancer Res.*, 1957, **17**, 1098.
[9] Pruitt, J. C., Hilberg, A. W., and Kaiser, R. F., *New Engl. J. Med.*, 1958, **259**, 1161.
[10] Shimkin, M. B., and Moore, G. E., *J. Amer. med. Ass.*, 1958, **167**, 1710.

number of takes; but, the more cancer cells injected, the less effective HN2 was. Applying this knowledge to human patients, they found that refinement of technique enabled malignant cells to be detected both in the venous blood draining a tumour and in the systemic veins in a "surprisingly large" number of patients. The number of cells was much greater for inoperable than for operable cancers—for example, in 50% of 14 inoperable cases and 4.6% of 65 operable cases operative manipulation of a tumour was found to result in an increase in the output of cancer cells; wound washings in 100 major resections showed undoubted malignant cells in 34% and suspicious cells in a further 18% of cases. Unfortunately, HN2 given at operation added considerably to the dangers of a major resection, both immediately and later, because of leucopenia. A further piece of experimental work, by D. M. Shapiro and colleagues,[8] showed that in breast cancer in mice there was an inverse relationship between the number of solid cancer cells and the chemotherapeutic effect of 6-mercaptopurine. Not only was a larger tumour less responsive but it appeared to be able to protect smaller tumours in the same animal from damage by chemotherapy.

Pathologists are becoming more skilful at finding malignant cells in the blood stream, and many contemporary articles testify to this achievement. As an example, figures published by Pruitt and colleagues[9] may be quoted. Using a technique which entails the addition of streptolysin-O as haemolysin and leukocidin followed by passage of the resultant material through five or six Millipore filters, they found cytologically malignant cells in 39%, and suspicious cells in a further 12%, of 100 patients with known cancer, whereas in 200 control patients there was only one case in which suspicious cells were identified. It is too early as yet to assess the diagnostic as opposed to the prognostic significance of such observations.

At the International Cancer Congress in London last summer some references were made to this matter, and now from the United States comes news of a project sponsored by the National Cancer Institute.[10] No fewer than forty-eight departments of surgery of Veterans Administration hospitals have agreed to co-operate in a statistically controlled clinical study on the adjuvant use of chemotherapy in the surgical treatment of cancer. Two investigations are under way, the first using thio-T.E.P.A. in resectable cancer of the stomach, the second HN2 in resectable cancer of the lung. The objects of the survey are: (1) to establish whether there will be improvements in end-results of treatment; (2) to ascertain if drugs which are palliative in advanced disease may be curable in early stages; and (3) to develop methods and techniques for therapeutic trials in cancer in general. Although experimental animals in common use are known to respond to these two drugs, a criticism which may be suggested of this proposal is that human patients suffering from carcinoma of the stomach and bronchus have so far shown no signs of responding to such treatment. It is therefore difficult to see why the drugs should be any more effective when given at the time of operation than at a later stage. Nevertheless, the sponsors of this scheme are to be congratulated. For far too long individuals have spent their short clinical lives struggling to achieve advances with limited numbers of patients. Surely it is only by corporate efforts on such a scale as this that real advances in the treatment of human cancer can be gained. Perhaps the British Empire Cancer Campaign may consider this sort of thing and clinicians be forthcoming to plan such research.

PRESSURE ON THE DRUM

Otitic barotrauma is still a not unusual hazard of flying in non-pressurized aeroplanes, though nowadays it happens seldom in pressurized aircraft. In military jet-propelled machines, with their capacity to make large and rapid changes in height, aural discomfort is relatively common. The disorder is due to a failure of equalization of the air pressures on each side of the drum membrane because of an obstruction in the eustachian tube or a functional derangement in the muscles surrounding its pharyngeal orifice. The usual cause is the common cold, with resulting swelling of the mucosa lining the tube and an excess of secretion; together these may partly or wholly obstruct the lumen of the tube, preventing air passing along it when the pharyngeal orifice opens during swallowing. Air is thus trapped in the tympanic cavity and is slowly absorbed, gradually reducing the pressure on the inner side of the drum membrane. Variations of pressure on the outer side may then cause symptoms. The worst effects are felt during descent, since the pressure increases on the outer surface of the tympanic membrane, driving it towards the inner wall of the tympanum, and finally holding it in a position where reinflation by the usual clinical manœuvres is impossible. This trauma results in a sero-sanguineous exudate into the tympanum and haemorrhages into the mucosa, and permanent damage may follow. The normal position of the drum can be restored by placing the patient in a decompression chamber and reducing the atmospheric pressure, but only if the eustachian tube is patent.

Unfortunately knowledge of the normal variations of pressure in the eustachian tube and the tympanic cavity is incomplete. K. Barbey and his colleagues[1] have recently published an account of a new method of studying and measuring these pressure changes. Each external auditory meatus is sealed by an inflatable cuff through which a rubber tube passes connecting the air space of the meatus with a polygraph and a transducer converting air pressures into electrical impulses. The nostrils are also occluded and the air pressures in the nasal cavity recorded in a similar way. This circuit includes a compressed-air container and a manometer, so that pressures in the nasal cavity, and therefore the nasopharynx, can be raised by a known

[1] Barbey, K., Oltersdorf, U., and Pauchinger, P., *Germ. med. Monthly*, 1958, 3, 215.

amount. After calibrating the three transducers to a common level, records are obtained (1) when swallowing with the nose closed; (2) during Valsalva's manœuvre; and (3) swallowing while the nasopharyngeal pressure is raised. The method is simple in principle and could well be fruitful in result. Unfortunately the recording amplifiers used by these workers came from electrocardiograph machines and were designed to record impulses and not prolonged responses. It would be unjustifiable, therefore, to draw firm conclusions from their results, but further work may be more rewarding.

PATENT MEDICINES ON TELEVISION

Anything that forces itself on the attention is apt to stir up mixed feelings, and advertisements are no exception. When they fill the breaks between and within television programmes, they find a captive audience that may be anything from inert to spellbound but is probably not very critical. It is therefore reassuring to see that the opening words of the Independent Television Authority's principles of advertising[1] state the "general principle" that it should be "legal, clean, honest and truthful." Clearly these are admirable precepts, and if they do not exclude the possibility of the advertisements also being "nonsense," as a correspondent calls them in a letter at p. 787, they are intended to prevent the use of "lies" and "half-truths," which the same correspondent detects in some of them.

In order to help the Authority maintain proper standards it has an advertisements committee, on which the B.M.A. has an experienced representative in Dr. H. Guy Dain. According to the Assistant Postmaster-General, who recently replied[2] to some Parliamentary questions on the subject: "All advertisements and claims for these proprietary drugs are considered by the committee and would not be approved if they were wildly extravagant." Thus control is exercised over the advertising of medicines on television, and the criteria which the committee has to guide its judgments are generally accepted. Those relating specifically to medical products are set out in the British Code of Standards,[3] which apply to all advertising to the general public, and their more important provisions may be paraphrased as follows:

No advertisement should:

Contain a claim to cure.

Offer a product or advice relating to a disease for which the patient should rightly receive the attention of a registered medical practitioner.

Appeal to fear.

Offer diagnosis or treatment by correspondence.

Claim that the product could promote virility or prevent premature ageing.

Offer any medicinal product for the purposes of slimming, weight reduction, or figure control.

Offer diagnosis or treatment by hypnosis.

In addition, special limitations are imposed on products advertised for the treatment of baldness and haemorrhoids and on the use in advertisements of such words as "doctor," "hospital," "clinic," "laboratory." Parliament has also imposed certain statutory prohibitions, so that it is an offence to advertise, outside technical journals, a product as a remedy for cancer, tuberculosis, epilepsy or fits, Bright's disease, cataract, glaucoma, diabetes, locomotor ataxia, paralysis, and venereal diseases. Nor may any product be advertised in terms calculated to lead to its use for procuring a miscarriage.

Television attracts big money for the advertising of medicinal products. In the three months October to December, 1958, £1,342,932 was spent on crying these wares to the public.[4] This sum was about 9% of the total spent on television advertising in the same period. The medicinal products covered by this sum exclude toothpastes and cosmetics but include "hair treatment and hair oils." Much the largest group of medicinals is "aspirin and headache remedies," on which about £335,000 was spent in the three months. "Indigestion remedies" took up about £187,000 worth of space, or perhaps time, on the screen, and "laxatives" £127,000. In keeping with the season, £122,000 was spent on advertising "cough and cold remedies." The products which had most spent on their advertising in this period were "aspro" (£85,000), "Beecham's powders" (£67,000), "alka-seltzer" (£45,000), and, round about £20,000 to £35,000, "Veno's cough mixture," "Fynnon salts," "Beecham's pills," "Angiers supervite capsules," "phyllosan tablets," "phosferine tablets," and "sanatogen beverage."

BRITISH MEDICAL STUDENTS' TRUST

We print this week a letter appealing for funds for the British Medical Students' Trust. The aims of the Trust are to provide travel grants for students wishing to study at universities and hospitals abroad and to pay for sending delegates from the British Medical Students' Association to meetings of the International Federation of Medical Student Associations (I.F.M.S.A.). A sum to yield £1,000 to £2,000 a year is wanted. We commend this appeal wholeheartedly to the profession: not only are its objects admirable in themselves, but the B.M.S.A.—the body behind the Trust—has a well-deserved reputation for doing what it can to help itself before calling on others. Furthermore, the fact that a former Treasurer of the B.M.A. and the present Chairman of Council are co-signatories of the appeal is sufficient guarantee that the need is real.

This is the kind of effort which it is rewarding to support. There need be no fear that money subscribed will be used to subsidize cheap holidays abroad—valuable though such may be. Each applicant has to

[1] *Principles for Television Advertising*, Independent Television Authority, 1955.
[2] *Brit. med. J.*, 1959, **1**, 729.
[3] *British Code of Standards Relating to the Advertising of Medicines and Treatments*, 4th ed., 1958.
[4] *Statistical Review of Independent T.V. Advertising*, Vol. 4, No. 1, February, 1959.

satisfy the B.M.S.A. that the travel he proposes is truly vocational in purpose, and he must provide a letter from the dean of his medical school to confirm it. The grants themselves cannot be more than a small proportion of a student's total travelling expenses. Over the last four years the B.M.S.A. has had 143 applications for grants under its Student Travel Fund, and at a cost of a little over £500 has made it possible for 55 students to visit 17 foreign countries for study. More than one-half of this money came from student sources. The countries most commonly visited have been Denmark (19), U.S.A. (9), Norway (6), and Italy (5). Now the B.M.S.A. wants to extend this aid.

The B.M.S.A. is a lively body, carrying out much useful work on behalf of its members—some 90% of all medical students in Britain. It concerns itself closely with the medical curriculum, and has already published well-reasoned reports on the premedical and preclinical curricula, with one on the clinical curriculum to follow. It helps students with their State and local authority grants, and looks to their welfare generally. It publishes a journal, and at its annual meetings organizes symposia on topics of special interest to its members, the two most recent being on "The Teaching of Sexual and Marital Relationships to Medical Students" and "Entry into General Practice."

The international activities of the B.M.S.A. are important. Over the last four years the B.M.S.A. has found nearly £1,400 to send its delegates to meetings of the I.F.M.S.A.—and again most of the money has come from student sources. This year Britain has been chosen as Chairman Nation of the I.F.M.S.A., a Federation speaking for medical student associations in 24 countries. Only recently, too, the editing of the I.F.M.S.A.'s journal *Intermedica* has become a British responsibility. These honours show that the name of the B.M.S.A. stands high among similar organizations in other countries. If the Trust Fund receives the support it deserves, it will allow students from Britain to learn from their contemporaries abroad and will help the B.M.S.A. to contribute yet more effectively in the international field.

AORTIC SYSTOLIC MURMUR IN OLDER PATIENTS

In general, aortic systolic murmurs are of two kinds—those due to aortic stenosis and those due to aortic sclerosis. By aortic sclerosis is meant thickening of the base of the aortic cusps, which have become involved in calcific atheromatous disease of the aorta, but without fusion of the commissures and valvular stenosis.

Recently D. L. Bruns and L. G. Van der Hauwaert[1] examined 300 patients over the age of 50 in the general medical wards of a hospital, excluding those with rheumatic, luetic, or congenital heart disease, and detected a systolic murmur in 146 of these cases. The incidence of aortic systolic murmurs increased with age, for they found 37% in the 50 to 59 age group, 47% between 60 and 69, 66% between 70 and 79, and 69% between the ages of 80 and 89 years. Not only did the incidence of murmurs increase with age, but also the proportion of the murmurs that were loud. Phonocardiograms were recorded in 33 of these 300 patients, and the murmur was seen to end well before the second heart sound in every case and to be rhomboid in shape—that is to say, having a central crescendo. This pattern is similar to that seen in aortic stenosis, when, however, the murmur tends to be slightly longer if the stenosis is at all severe. In most of the patients the murmur was best heard over the second right intercostal space, but was also audible in a band down the sternum out towards the apex. The murmur was confined to the aortic area in 14 cases and to the apex in 22. In the remaining 110 cases the murmur was heard in both areas. It was often transmitted into the neck, but a thrill was seldom felt, being present in only three patients. Special note was taken of the presence of a hyperkinetic state, such as anaemia, thyrotoxicosis, or liver failure, or of associated hypertension, since these conditions by themselves may produce a murmur.

Necropsy evidence of the cause of the aortic systolic murmur was obtained in 23 of the 300 patients. Concurrently a special pathological examination of the heart was made in 168 subjects reaching necropsy during the present study, those with a valvular lesion being excluded. Some thickening of the cusps of the aortic valve was found in 120 of the 168 subjects. In mild cases it was fibrous and confined to the central region of the cusp, while in the more advanced cases it spread towards the free margin and there was associated calcification. In all, the free margin of the valve was fully mobile and there was no fusion of the commissures. Great valve thickening was seen only in the older subjects, though not all the older people showed this change. Slight thickening was seen quite frequently from the age of 40 onwards.

Since both thickening of the aortic valve and an aortic systolic murmur were increasingly frequent in the older age groups, it was concluded that aortic-valve thickening without stenosis was probably the cause of the murmur in these patients. This view was supported by the necropsy findings in the 23 patients, who had also been examined by the authors clinically. It was noted, however, that in those patients who had a higher than normal cardiac output the murmur was louder than would have been expected from the degree of aortic-valve thickening.

The benign nature of the systolic murmur of aortic sclerosis needs to be recognized and special care taken to distinguish it from the murmur of aortic stenosis, with its more serious prognosis. Points which may help in the diagnosis are the age of the patient, for if he is of advanced age aortic sclerosis becomes the likely diagnosis; and, secondly, symptoms of reduced left ventricular output and left ventricular strain, which point to aortic stenosis.

[1] Bruns, D. L., and Van der Hauwaert, L. G., *Brit. Heart J.*, 1958, **20**, 370.

Drug Treatment of Disease

MYASTHENIA GRAVIS

BY

J. W. ALDREN TURNER, D.M., F.R.C.P.

Neurologist, St. Bartholomew's Hospital

Effective drug treatment of myasthenia gravis was introduced in 1934 when Dr. Mary Walker discovered that an injection of physostigmine would relieve the muscular weakness of the disease. In the following year she found that neostigmine had a similar action, and as it is more effective and less apt to cause side-effects it is now the standard drug used in treatment. In myasthenia gravis there are no recognized histological abnormalities in the central nervous system, the peripheral nerves, or the skeletal muscles, with the possible exception of slight changes at the motor end plates. The disorder is thought to be due to a disturbance of conduction at the neuromuscular junction, the exact nature of this being still undecided. Neostigmine is an inhibitor of the enzyme choline esterase, which inactivates acetylcholine, and it is partly owing to this action that the drug improves muscular power in myasthenia gravis, but there is also some evidence that it exerts a direct action on voluntary muscle fibres.

Neostigmine

Neostigmine can be given by the mouth as neostigmine bromide, each tablet containing 15 mg., or by subcutaneous injection as neostigmine methylsulphate in doses of 0.5 to 2.5 mg.; 15 mg. by the mouth is approximately equivalent to 0.5 mg. by injection.

Oral Treatment with Neostigmine.—Most patients on neostigmine receive it by mouth. The dosage varies considerably in accordance with the severity of the disease, and often it may have to be varied from day to day, this depending on the patient's activities. Oral neostigmine increases power in about thirty minutes, and the effect usually lasts from three to four hours. Doses therefore have to be given at regular intervals of about three hours, though some patients find it more satisfactory to have two-hourly or even hourly doses. Many myasthenic patients have difficulty in swallowing and sometimes in chewing, and for this reason doses are best given about half an hour before meals; even for patients without bulbar disease this is the best procedure, because neostigmine has a greater effect when taken before meals. If it causes nausea, some milk or a biscuit can be taken at the same time. Because of the short action of the drug a dose should be taken last thing at night and immediately on waking (when muscle weakness is often marked), and in severe cases a dose will have to be taken during the night.

In starting treatment of a patient it is usual to begin with a small dose such as 15 mg. three- or four-hourly during the day, and by trial adjust the amount used and the timing of the drug to get the maximum benefit without causing serious side-effects. Co-operation from the patient is most important in achieving this. The total dosage varies greatly, so much as 1,000–1,200 mg. in 24 hours being needed for short periods in some patients.

Neostigmine by Injection. — An injection of neostigmine is of great value as a diagnostic test in myasthenia gravis, 1.5 mg. together with atropine 1/100 gr. (0.65 mg.) being given subcutaneously. In myasthenia there is considerable and sometimes dramatic improvement in power. The effects last for about three hours. This marked increase in power after a neostigmine injection does not occur in other conditions causing weakness of muscle, though slight improvement may be seen in a variety of diseases. In some cases of myasthenia gravis, particularly those of long standing, the weakness may not be completely relieved; this is especially true of the external ocular muscles, a fact which must be realized in assessing the results of a diagnostic injection of neostigmine. In normal people, and those with other diseases, 1.5 mg. of neostigmine by injection may cause widespread muscle fasciculation, which does not occur in patients with myasthenia.

Injections of neostigmine are not needed in the treatment of most myasthenic patients, but they may be useful before an exceptional increase of activity or during an acute infection, such as pneumonia, which often aggravates myasthenia. In a myasthenic crisis or immediately after thymectomy, neostigmine should be given by injection, and to secure a continuous effect it can be given in a slow intravenous drip.

Side-effects of Neostigmine. — Neostigmine may produce side-effects. By its muscarinic action it causes contraction of the smooth muscles of the alimentary tract, resulting in colicky abdominal action, pain, nausea, vomiting, and diarrhoea, and by its similar action on glands produces salivation, lacrimation, sweating, and increase of bronchial secretions. In some myasthenic patients, particularly in the early stages of treatment, abdominal pain, nausea, and diarrhoea occur, and these troublesome symptoms can usually be controlled by the oral administration of tinct. belladonnae, 10–15 minims (0.6–0.9 ml.) or ext. belladonnae sicc., ¼ gr. (32 mg.) three times a day, or in my experience preferably by propantheline bromide, 15 mg. two or three times a day. When neostigmine is given by injection it is advisable to give atropine also in a dose of 1/100 gr. (0.65 mg.), the frequency of injections being adjusted to prevent the abdominal symptoms.

A more serious effect which occasionally occurs in myasthenia when large doses of neostigmine are given is due to the nicotinic action of the drug, which may cause widespread fasciculation and increased weakness of voluntary muscles. This condition, sometimes called a cholinergic crisis (to distinguish it from a myasthenic crisis), can usually be recognized because the increased weakness comes on within 15 to 45 minutes of administration of neostigmine and is accompanied by muscle fasciculation, salivation, increase of bronchial secretions, small pupils, and frequently coldness and clamminess.

Some workers have found the "tensilon" test valuable in distinguishing between a cholinergic and a myasthenic crisis. Tensilon (edrophonium chloride) is a

very short-acting anticholinesterase drug; when it is given intravenously, myasthenic weakness improves in 30–40 seconds and the increase in strength lasts about five minutes. However, when it is injected into a patient in a cholinergic crisis there is temporary aggravation of the muscle weakness. This test probably has some value in differentiating the two types of crisis, but it may be difficult to evaluate the result owing to the very short action of the drug.

If a cholinergic crisis (due to overdosage of neostigmine) occurs, administration of the drug must be stopped temporarily, atropine should be given in a dose of 1/60 gr. (1 mg.) intramuscularly, and this dose repeated hourly until signs of atropinization occur. Measures must also be taken to treat weakness of bulbar and respiratory muscles, such as tracheal intubation, tracheotomy with positive-pressure respiration, or assisted breathing in a respirator, depending on the distribution of the muscle weakness.

Pyridostigmine

One of the main disadvantages of neostigmine is its short action, and pyridostigmine ("mestinon"), a pyridine analogue of neostigmine, was introduced in 1954 as it was said to have a rather longer action and was less apt to cause side-effects on the alimentary canal than neostigmine. A 60-mg. tablet of pyridostigmine by mouth corresponds to 15 mg. of neostigmine. The total dosage and timing of their administration is worked out as described for neostigmine. In general, pyridostigmine produces side-effects less frequently and is the more useful drug for the control of myasthenia gravis, but individual patients vary in their response and some prefer to continue with neostigmine. In others a combination of the two drugs gives the best results, neostigmine being used during the day and pyridostigmine for the last dose at night, as its rather longer action may obviate the need for a dose during the night in the more severe cases.

Other Drugs

Organic Phosphate Compounds.—During the past twelve years several long-acting choline esterase inhibitors have been tried in the treatment of myasthenia gravis; the best known are di-isopropyl fluorophosphate (D.F.P.), tetraethylpyrophosphate (T.E.P.T.), and octamethyl pyrophosphoramide (O.M.P.A.). These drugs were found to be uncertain in their action, and toxic effects were frequent and difficult to control. There does not seem to be any place for them in the routine treatment of the disease.

Ephedrine has some effect in increasing muscle power in myasthenia, but the mechanism of this is uncertain. It can be given in a dose of ½ gr. (25 mg.) two or three times a day in addition to neostigmine or pyridostigmine. In my experience it has proved most useful in patients who wake during the night with choking and respiratory difficulty, and it seems likely here that its main value is from its bronchodilator effect.

Drugs to be Avoided

Quinine aggravates myasthenia, an effect opposite to that seen in myotonia, where the delayed relaxation of muscle is often relieved by quinine and aggravated by neostigmine. Myasthenic patients are very sensitive to curare, and this drug should not be administered in operations on patients with the disease unless this danger is realized and adequate provision made for assisted respiration until the effects of the curare have worn off. A.C.T.H. and cortisone have been given in the treatment of myasthenia, but they often exacerbate the disease after a few days; a remission sometimes occurs after the drug has been stopped. In view of this, great care should be taken in using these drugs for a coincidental disease in a myasthenic patient.

Treatment Apart from Drugs

About 12% of myasthenic patients have a neoplasm of the thymus. It can usually be shown radiologically by screening of the chest, antero-posterior and lateral pictures, and if necessary tomography. These patients should be given deep *x*-ray therapy to the tumour, and in some cases operative removal of the thymoma should be carried out at a later date. During deep *x*-ray treatment the necessary dosage of neostigmine may vary considerably from day to day and careful supervision of this is needed. The question of operative removal of the thymus in myasthenia patients who have not got a radiologically demonstrable thymoma has been discussed recently in a leading article in this *Journal* (1959). In general the operation should be carried out in patients under the age of 45–50 if the disease is becoming generalized, or progressively getting worse, and if the patient is needing increasing doses of neostigmine or pyridostigmine and notable remissions are not occurring. In exacerbations of the disease, when there is bulbar palsy or paralysis of the respiratory muscles, the patient needs treatment by methods similar to those used in poliomyelitis or acute infective polyneuritis—namely, postural drainage, physiotherapy to the chest, and in some cases tracheotomy and positive - pressure respiration.

REFERENCE

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REACTIONS OF CANCER PATIENTS ON BEING TOLD THEIR DIAGNOSIS

BY

JEAN AITKEN-SWAN, A.M.I.A., A.H.A.

AND

E. C. EASSON, M.D., F.F.R., D.M.R.T.

Christie Hospital and Holt Radium Institute, Manchester

"I asked the doctor—I looked him straight in the face and I asked 'Is it cancer?' and he said, 'Yes.' Well, I'd rather know the truth—it's better than imagining all the time. I asked my own doctor in the first place, 'was it . . . ?' and I didn't get to say the word, and he said 'We don't know,' so naturally I thought it must be. If I'm ill I'd rather know what I'm suffering from, because you don't die any sooner for knowing about it."

Doctors and journalists sometimes discuss what the patient with serious disease should be told about his illness. The patient's own views are seldom heard. It is generally assumed that patients with cancer, even those with localized and curable conditions, prefer not to be told the diagnosis, and that silence or reassurance is the best solution to the patient's (and doctor's) anxiety. This policy has unfortunate repercussions for cancer education. It means that the only cancer patients

most people know are those with advanced disease who die. If the patient does well the condition, it is thought, cannot have been cancer. This masks the more optimistic side of cancer treatment and so encourages a fatalistic attitude, resulting in delay in seeking advice through fear.

The study analysed in this paper started with the premise that it was in the public interest for early cancer likely to be cured to be quite unemotionally and casually referred to as "cancer" from the beginning. In this way a nucleus of patients would be created with no doubt in their minds about what had been the disease. In the event, as will be seen later, the surprising finding was reached that in the large majority of cases such telling was what the patients themselves preferred. In all, consultants told, and recorded having told, 231 selected patients (Table I).

TABLE I

Site of Lesion	Male	Female
Skin or lip	79	53
Mouth or tongue	13	9
Uterus	—	63
Breast	—	11
Other	1	2
	93	138

Patients' Initial Reaction

Between a week and a month later, depending on the patient's availability, and in the course of an interview ostensibly centred on the medical history, one of us (J. A.-S.) tried to discover indirectly the nature of the patient's reaction to the consultant's explanation. Many interviews were recorded, always with the patient's knowledge. Towards the end of the inquiry it was decided to seek the family doctor's views (35 cases), and to interview as many patients as possible a second time. Those who were being followed up at distant clinics, who had been dismissed, or who were on written follow-up could not be seen again. In all, 41 were seen a second time from one to two and a half years after having been told, in order to learn what they then thought and if they had spoken of their condition as cancer to others. This last was an important factor if "telling the diagnosis" was to have any educational value.

Given an indirect approach, sympathetic listening, and some encouragement, it was hoped that patients would feel free to speak of any worries, as indeed many did. The results of the inquiry are summarized in Table II.

TABLE II.—*Patients' Initial Reaction*

Reaction	Male	Female
Approval	61	92
Denial that they had been told	23	21
Disapproval	0	17
Inconclusive*	9	8

* This group tended only to respond to direct questions, and no conclusions could be drawn about them.

Approval

1. "I think you go through your treatment better because you know it's a case of life or death with you. You couldn't get better without it, could you? That's why I wanted to know. I think it's very—wise—to know, yourself; it wouldn't do to tell anyone else. Though I think a lot of people here think they have got an abscess—well, it's just as well to let them think so." Later she said: "I think it's better to tell people, because I think it makes them fight better."

2. "I'm the worrying sort—that's just it. If I'd asked the doctor and he'd brushed me off it would have been worrying. I'd sooner he told me when he wanted me to go to Christie's. I would advise a doctor to be frank unless, of course, it's an internal one, and then I should be very, very careful, because it could come as a nasty shock and they've got to have the will to carry on. If he tells them when it's on the bladder or somewhere internal which means a serious operation, they might just—give up. But with these curable things I do think it's best to tell them what it is, and the seriousness of the treatment, so that they'll go in for it and do what they're told and not stray."

These two patients stress the practical value of knowing, suggesting that they submit to treatment in a different spirit if they know. Other patients make it clear that to be told nothing or to be reassured and yet to be treated at a cancer hospital is more worrying than to be told frankly what is wrong.

3. "It took the use of my legs when he told me. But I'd much prefer to know, and then you know what you're fighting. If they don't tell you you just keep worrying and wondering 'Have I got it?'; so it's much better to know. In my ward, of course, I'm the only one that's got it. They say 'What's the matter with you?' and I say 'I've got an early cancer of the womb, what's the matter with you?' and they say, 'Oh, I've got a growth, I've got an ulcer, I've got this and that.' Don't you think people can fight things better if they know?"

4. "If you know what's the matter you know what to expect, but if you're in the dark and they're treating you for this and that and you don't really know, it worries you more. I mean I wasn't shocked. It stunned me a little, but I wasn't really afraid. Of course, I was upset when I came in, but I'm not now." "What upset you?" "I think it was self-pity. When you've no one to talk to it worries you."

Patients are usually well aware that the truth is sometimes concealed from them.

5. "When we have this we always wonder how much is being kept back and how much is being told for our own good, you know."

6. "I would probably not have been reassured if the doctor had said it was nothing. But I know of people who have been reassured that it could be cured, and the doctor has told their relatives that nothing could be done. That worries me."

7. "I heard the doctor say it could be a small cancer—now, that was the first I knew, and it didn't cause any shock or worry or anything. You see, there's this way of looking at it. If a person knows the truth at the beginning it's a pleasant surprise if it's not so bad when the time comes, and it isn't a shock if it is. You're always capable—and maybe there's a chance—of hearing good news if the patient is told the truth. It's no good making a mystery of it, is there? A person worries more if it's a mystery. And people will never get to know that cancer is ever cured if they're never told what it is."

Most of these patients add that only those whose condition is curable should be told, in their opinion, and their thinking invariably stops at this point.

Denial

Denial that they have been told was the reaction of 19% of the patients, and of more men than women. After the patient had given all the information he meant to give freely without having mentioned cancer or what he was told, a direct question had to be asked about the possibility of the condition being cancer and if the consultant had said anything about this. Denial was therefore definite and not due to misunderstandings. Sometimes the patient would not use the word cancer

until after the interviewer had introduced it. In no case did the interviewer question the patient's claim not to have been told.

8. "The doctor didn't say it was cancer. He just said it was in an early stage and could be cured. I didn't ask, because if I don't know I won't worry, will I?"

9. "The doctor didn't say what it was. They don't tell you anything, and when they're so nice with you you don't like asking in case it seems cheeky."

10. "He said I had an ulcer on the neck of the womb, he said, and 'we can cure it.' So that made me feel better—yes, that made me very comfortable." To introduce the word the interviewer said: "You mean that coming to Christie's you had thought it must be cancer?" "Yes, I did. I asked him if it was a cancer" (at this point her eyes filled with tears), "but he said 'Not at all, it's just a small ulcer.'" In his letter to the family doctor the consultant had said that this patient had been told and that she had accepted the diagnosis quite happily.

Disapproval

Few give any indication that they disapprove of being told frankly the nature of their complaint—only 7%, and all women. Not all say so in so many words, because, after all, there is an element of self-esteem involved. Some are contradictory.

11. "I've died many deaths since he told me. I suppose I asked 'Is it cancer? having to go to Christie's,' and he said 'Yes, it is, but it is localized,' and I think he said it was early and that I had a fair chance or a good chance—I'm not sure which. I can tell you it was a shock—I nearly died. I think he was over-frank with me."

12. "My doctor told me it was an ulcer on the womb and that I needed treatment. I think it should have been left at that. There was no need to tell me what it was. It's the word that is so terrible."

13. "He said it was a simple cancer of the skin. It was a terrible shock—I went all dizzy. I had never thought of such a thing. Well, it is the *word*! I've had diarrhoea ever since and haven't slept at all, thinking about it and imagining things." "Would you rather the doctor had not told you?" "Yes, I would. It has upset me so much. He could have said it was a cyst or something."

Patients' Delayed Reactions

Of the 41 patients who had been seen one to two and a half years after the first interview, 35 had not changed their views, five had, and one who denied that she had been told now talked freely of her condition as cancer (Table III).

TABLE III.—*Patients' Delayed Reactions*

At First Interview	Total	At Second Interview			
		Approved	Disapproved	Denied	No Longer Denied
Approved ..	32	29	3		
Disapproved ..	5	2	3		
Denied	4			3	1
	41	31	6	3	1

Of the 37 who did not deny that they had cancer, 26 did not mind others knowing that they had had cancer, 10 had not let anyone know, and the attitude of one on this point was not clear.

14. The consultant noted: "When I disclosed the diagnosis to this patient she expressed more horror than any other patient I have seen so far. 'It is that awful word!' In the end she seemed glad to know, especially since I could reassure her as to cure." The patient's story was: "He told me what it was—a skin cancer like spinners get. Terrible, terrible! I was terribly upset. But I have every confidence in him." "Because he told you so frankly?" "No, because of the way he looked at me—so kind. I just stared at him when he told me—I seemed calm when I left the hospital, but inside—!" "Were you upset because you thought it couldn't be cured?" "No, I wasn't worried about that. It just seemed such a terrible thing to be carrying around with me. I'm glad he told me, because I've known to take care of it, and I might not have bothered if I'd thought it was nothing." About two and a half years later she still approved of having been told. "I think the most valuable part of knowing about it is that if you have anything similar you know how to pay attention to it." She had persuaded a relative to seek advice for a similar lesion, and he had also been treated at this hospital. "I don't mind people knowing," she said. "I would tell anyone."

15. This patient described herself as "one of a well-known family" in her village, "and things soon get around there." She had never heard of cancer being cured, so it had been a great shock when the consultant told her she had an early cancer of the womb. "With the cases I'd known I'd given myself up." Two years later she was in again, cheerful and chatty. "I had given myself up," she said. "When he said I was to come in for two weeks I thought 'They'll say anything to get you in.'" "You didn't believe him when he said it could be cured?" "No, I didn't really. But I thought it's either kill or cure and I'd better go." She still thought it better for the doctor to be frank. "Yes, I do; otherwise I might not have gone. And I look at it like this—it helps other people too. I'm a talkative sort—well, you can see I am—and I tell people about my experience, and it helps them if they're frightened about Christie's. I belong to an old folks' club and we get talking there, and when I sit in the park I talk to the people on the same seat, as old people do, and I tell them, and I think it helps."

16. Seen two years later, another patient said that, looking back, she would rather not have known. "Not with them at [referring] hospital telling me it was a cyst. Then to come here and be told it was a cancer made me lose faith in doctors speaking the truth at all. If they reassure me about anything again I just wouldn't believe them." Later she said: "It wouldn't be fair to the hospital not to tell everyone what I've had. But they can hardly believe me."

Two points are repeated by many of the patients. They are aware of the educational effect of what they say. "I think it's only right to tell other people," said one. "It's only fair to the hospital when they've cured me of cancer," said another. Then they say how sceptical their friends are about their having had cancer at all. "She didn't believe me—she said they'd never tell you. I said 'Well, I wouldn't make it up, because it's not a nice thing to have had.'" Another said: "I said to one lady what I'd had, and she said that wasn't cancer—it was a growth, perhaps. She was really indignant about it. People are funny. Another lady I mentioned it to could hardly credit it." Another said: "They think I'm romancing." Such is the popular conviction that doctors do not tell the truth to patients with cancer.

Ten patients seen a second time had not spoken of it to their friends.

17. An old woman thought it was all right to be told so long as the condition could be cured. "If you're not told and do get to know it comes as more of a shock." After treatment she did not tell her sister or the people she lived with about it. "I'll see how I go on," she thought, "people are funny." A year later she said she had still kept it to herself. "Well, you see, love, I thought they might shun me."

18. Another did not really believe that she was cured. Asked if she had never heard of anyone cured of cancer, she said very positively: "*Never* in my life, and I can't

really think it can be. . . . Well, the doctor said it was a cure. I said, 'Are you sure, doctor?' and he said 'Yes.' And yet I can't convince myself that nobody can get cured." Speaking of having been afraid, when in hospital a year before, that her friends would get to know that it was the Christie Hospital, she said: "Well, I am now . . . well, I'm like this. If I hear of anyone talking of this place I say I know a friend and they've done well for her—and it's myself all the time. No, I'm too sensitive. I wouldn't like them to think I've had anything like that."

The Family Doctor's Point of View

In 35 cases, after the patient had returned home after treatment, the family doctor was sent a questionary asking: (1) Did the patient discuss with you the diagnosis he was given here? (2) What was his reaction? (3) Your comments.

The majority of patients who, according to our classification, approved of being told the diagnosis did discuss it with their doctor. Four out of five who denied to the interviewer that they were told did not discuss it with their doctor either. In reply to "What was his reaction?" the doctors made such comments as: "Not worried," "Sensible," "Quite philosophic about the whole thing," "Grateful for the information." In no case did the family doctor report an unfavourable reaction to being told. Their comments were: "I feel in this case everything has been gained and nothing lost by telling the patient the exact nature of the lesion." "This patient took the diagnosis well. She will not in future hide any symptoms, and I should think would be less alarmed by any proposed treatment than before." "I approve the policy adopted in early cases like this patient." "I think it a good idea, certainly from the G.P.'s point of view. Most patients of mine who have known the truth have been far easier to deal with and happier."

The Problem of Telling

So far we have been analysing the patients' reactions to having been told. A short comment is also indicated on the experience of the consultants who told these patients their diagnosis.

Medical men are not endowed with special courage, and they have not themselves been insulated from the accumulation of human experience on which the fear of cancer is based. There is therefore a reluctance, variously rationalized, to talk freely to patients about cancer, even when cure presents little problem. However, fortified by the motive of public education, frankness with these patients has become progressively easier with each case, and indeed the customary atmosphere of "therapeutic deception" has been replaced by a refreshing honesty, advantageous to doctor and patient alike.

It was an essential feature of this experiment to tell the patient his diagnosis in the most matter-of-fact way possible, indicating almost in passing that cure was taken for granted. "This ulcer on your tongue, Mr. —, is quite a typical and straightforward cancer, a cancer of the tongue. It's a small one, of course, so we can easily get rid of it for you. Permanent cure of this sort of cancer is not difficult—because you were a very wise man to consult your doctor while the cancer was still so early." Some discussion of treatment follows—how, when, and where.

The immediate reactions of these patients in the out-patient department, where most of them were told their diagnosis, were remarkably placid and forthright, whatever the ultimate finding at the later interview. Some asked for further reassurance as to cure, some about infection of others, or about heredity. Only one or two patients in the entire series reacted there and then with emotional instability. This type of patient can sometimes be spotted beforehand, and would probably be better left in ignorance.

Discussion

There is no doubt that in this country the word cancer connotes incurable disease with distressing and inevitable death. This fact must surely have its origin in experience, and only new experience rather than exhortation and reassurance will alter this conviction. It has long been British medical practice to conceal from patients that they have cancer, with the consequence that the only diseases known as cancers were uncured or untreated ones. The cured cases were scrupulously labelled as anything other than cancer. The effect of this "heads-I-win, tails-you-lose" policy is evident from the incredulity of patients' friends when told the truth. This general ignorance of the very possibility of cure was also shown by an opinion survey in the Manchester area (Paterson and Aitken-Swan, 1954), when 64% of those interviewed did not know that cancer could be cured.

It would seem, therefore, to be an essential part of successful public education on cancer, and in the general interest, that some patients with the more curable types of growth should be told the diagnosis. By the same reasoning those already cured should likewise have the facts presented to them, but by then the effect is much less. If frankness of this sort could be shown, however, to have unexpected and undesirable sequelae then such a policy would have to be abandoned, however good the motive may seem for its continuance. The contrary seems to have been established.

Lack of space limits the full evidence being presented, but extracts have been selected to represent all points of view. So far as can be discovered, two-thirds of the group preferred to know what was wrong. This proportion, naturally, may only measure the success of the consultants' judgment in deciding whom to tell, but the fact remains that they seemed genuinely glad to know. In some cases "telling the diagnosis" had the effect of calming fears, the patient having interpreted silence or reassurance, while being referred to a cancer-treating hospital, as meaning that his case was hopeless. Others felt that to know the truth helped them to fight better, it gave them additional resources to call on, they submitted to treatment in a different spirit, and they worried less.

In a different category are those 7% who claimed to have been upset by the knowledge of their diagnosis. Some of those who denied they were told may also come into this category. In some cases it was said that the frank use of "the word" was what shocked them, rather than fear that they had an incurable disease, which is, of course, of itself indicative of an unhealthy state of public opinion. Some admitted that they would have preferred a lie. Not enough were interviewed later to draw any conclusions about how these patients eventually adjusted to their knowledge, but it seems reasonable to hope that what the word symbolizes to them, and the element of stigma apparently attaching to it, may be modified in time as they continue well and pain-free. From what patients have said, there is clearly more to this reaction than the inability to accept

the consultant's assurance that the condition is curable. Interviewing on a less superficial level would be required in order to learn more about why this group of patients with curable cancers found the knowledge of their diagnosis emotionally intolerable.

The denial reaction merits further study and follow-up. Patients who deny that they were told may be doing so because they did not "take in" what the consultant said. They at least could have had no undue reaction to the unsuccessful offer of truth. They may, on the other hand, have had a shock and not wish to be reminded of it, in which case they are merely denying to the interviewer that they were told. But in some cases they seem to be denying it to themselves as well—the same defensive denial encountered in some patients discussing their delay in seeking advice (Aitken-Swan and Paterson, 1955).

In basing these results upon the patient's own description of his reaction we are very conscious of the deficiencies of the evidence. What is said at an interview is inevitably the product of that particular situation and of the interpersonal relationship achieved by those two people. A low "disapproval" rate could in part measure the interviewer's failure to create the kind of atmosphere in which a diffident patient feels free to speak frankly. Also, misinterpretation is possible in the interviewer's attempt to sense the truth of the emotions behind the patient's words.

Throughout, the emphasis of the study has been on the patient's own words. We have had to omit from our quotations all that does not pertain to the subject under discussion, with a resulting appearance of over-simplification. But the interviews were, in fact, lengthy, and one part added to the understanding of another. Most important, perhaps, patients did not know that we were specially interested in what they had been told, and their freedom in expressing their reactions to this is some measure of success in establishing a friendly atmosphere. Finally, in those cases where the family doctor also reported, it was encouraging to see that, with few exceptions, his comments supported the impression that had already been formed.

Conclusion

It would of course be nonsense in the present state of British public opinion to expect all patients to approve the policy of being told their true diagnosis. If the given figures are accepted what must now be decided is whether a 7% disapproval rate is low enough to justify continuing this practice. Having regard to the very great advantages shown to be gained, both in the medical management of these patients and in public education on cancer, it is considered that 7% is a small premium to pay. It must be remembered, too, that this small group of patients, however critical they may be of the consultant's frankness, have almost certainly had their cancers cured. Moreover, it seems likely that this figure will fall still lower than 7% as public experience grows and public opinion changes.

To conclude, our results find striking support in the words of Dr. V. R. Khanolkar, speaking recently on British television. Discussing the problem of what patients with cancer should be told, he said: "Much against our expectations, shall we say, my colleagues and I were surprised that when the disease is more or less curable the patient has co-operated much more

(*Continued at foot of next column*)

(*Continued from preceding column*)

willingly when we have told him what the disease is, that something can be done for it, and that there is every hope of it being cured. . . . That is because I believe there is a very large fund of courage and resolution in human minds which we have not accounted for in the past."

Summary

A study is presented of the reactions of 231 selected patients who were told they had curable cancer. Two-thirds said they were glad to know the truth, 19% denied they had been told, while only 7% (all women) resented the consultant's frankness. The family doctors of 35 patients reported no untoward effects of this knowledge and none opposed the general policy of telling such patients their diagnosis.

It is concluded that since a sufficiently large majority of patients are able to accept the truth, and benefit from the knowledge, all patients with the more curable cancers, unless obviously unstable, should be told their diagnosis. This is considered an essential part of public education on cancer, aiming at earlier treatment and higher cure rates.

References

Aitken-Swan, J., and Paterson, R. (1955). *Brit. med. J.*, **1**, 623.
Paterson, R., and Aitken-Swan, J. (1954). *Lancet*, **2**, 857.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Brontyl (Lloyd-Hamol).—This is 7-(2-β-hydroxypropyl)-theophylline. Tablets of 120 mg. and ampoules of 300 mg. in 2 ml. are available.

The drug has been introduced to overcome the disadvantages of existing theophylline preparations, which arise because of the poor solubility of theophylline in water; this has necessitated administration of theophylline in the form of salts, such as the ethylenediamine salt (aminophylline). Ethylenediamine is itself toxic; moreover, free theophylline is precipitated from such compounds by the stomach acid, causing severe gastric irritation and preventing absorption. The hydroxypropyl derivative dissolves in water to give concentrated heat-stable solutions which are almost neutral. They are less painful when injected, and theophylline is not precipitated in the stomach. Brontyl may be used like theophylline as a bronchodilator, coronary vasodilator, and diuretic. One to four 120-mg. tablets are given 3–4 times a day. The ampoules are intended for intramuscular or intravenous injection in emergencies.

N.H.S. basic price: 100 tabs., 13s. 8d.; 5 ampoules, 6s. 6d.

Secrosteron (British Drug Houses).—This is dimethisterone), or 6α:21-dimethylethisterone, and is supplied in 5-mg. tablets. It is an orally active progestogen which, in comparisons made by animal experiments, has been found to be about twelve times as potent as ethisterone. Its relative potency in the human subject has not yet been accurately determined, and, since some other agents found to be highly active in animals proved to be only weak progestogens in humans, the place of dimethisterone in clinical practice remains to be shown. The manufacturers suggest that the indications for dimethisterone are the usual ones for progestogen therapy, and recommend a dosage of 1–3 tablets daily. However, it is best to review this in the light of any published reports.

N.H.S. basic price: 100 tabs., 75s.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

British Medical Students' Trust

SIR,—May we be allowed to draw your readers' attention to an appeal for funds now being made by the Trustees of the above Trust? The aims of the Trust are to give financial aid to medical students wishing to study abroad, and to defray the expenses of delegates sent to meetings of the International Federation of Medical Student Associations.

Until this year the Student Travel Fund of the British Medical Students' Association made available what moneys it had to assist medical students to travel for study. The greater part of money for such travel has been provided by the students themselves, and although well over £500 has been distributed in four years this is small when compared with the requests for assistance. For this reason the British Medical Students' Trust has been established and is now launching an appeal to provide a capital sum to finance the above objects.

Over 60 students have in the past been assisted to travel for vocational reasons. In all cases they have first to obtain the consent and approval of their deans. They have attended courses of study at universities and hospitals in Europe, especially those in Scandinavia, and in distant countries such as the U.S.A., Canada, Brazil, and Kenya. In taking part in such study courses these students have gained an early acquaintance with different philosophies and practice of medicine.

The British Medical Students' Association is a founder member of the International Federation of Medical Student Associations, a purely professional medical student body with a membership of approximately 180,000 students mostly from Commonwealth and European countries. This Federation receives the interest and support of the World Medical Association and the World Health Organization. Great Britain has always taken an active interest in the counsels of the Federation and this year has the honour of being the chairman nation. The Trust makes provision to allow a limited amount of money each year to defray the expenses of B.M.S.A. delegates to the meetings of the I.F.M.S.A.

The Trust, as far as we are aware, is the first of its kind in this country, in that it has been established by undergraduates to aid undergraduate education and welfare. The Trustees hope that members of the medical profession may wish to contribute to this appeal, and contributions by gift or deed of covenant will be gratefully received by the Secretary, British Medical Students' Trust, B.M.A. House, Tavistock Square, London, W.C.1.—We are, etc.,

A. M. A. MOORE,
Chairman of Trustees;
Honorary President of B.M.S.A.

SOLOMON WAND,
Trustee; Chairman of B.M.A. Council.

GRAHAM D. LISTER,
Trustee; President, B.M.S.A.

London, W.C.1.

"Getting Married"

SIR,—I am writing as Chairman of the Christian Medical Fellowship, following a discussion in the last meeting of its committee. The committee members present were unanimously convinced that we are speaking for the vast majority of our 1,200 members when we write in support of Dr. Wand's action, in suspending further circulation of the booklet entitled "Getting Married," until the B.M.A. Council could discuss the matter later this month.

We are sure that Dr. Wand, and his advisers, were correct in anticipating that Christians of all shades of opinion will take great exception to the chapter by Dr. Eustace Chesser on p. 38 of the booklet and to the opening of the article by Dr. Roger Pilkington on p. 54. We are also convinced that little attention need be paid to those who talk of "Infringement of the liberty of the press," etc., when such a matter is not at issue. All the contributors to the booklet have ample liberty and scope to express themselves through many other channels, and happily the British press, as a whole, is relatively free. *The material point* is that the front cover of the booklet has a blue panel which carries the caption "Published by the British Medical Association." The Chairman and the Council of the B.M.A. have, therefore, every reason for being sensitive in a matter which concerns the good name of the Association.

In writing as above, however, we wish at the same time to add that there is much in the booklet which is excellent and which needs saying. Much of it is obviously most relevant to the outlook of large numbers of young people throughout the country. It was therefore a thousand pities that a right initiative by the B.M.A., and a good plan, should have been spoilt by unnecessary errors of judgment by the editor and two contributors to the booklet.—I am, etc.,

W. M. CAPPER,
Chairman, Christian Medical Fellowship.

London, W.C.1.

SIR,—You will, I am sure, allow opposite views to those expressed by your seven "worked-up" correspondents (*Journal*, March 14, pp. 714–715). I hold no brief either for Dr. Winifred de Kok or Dr. Eustace Chesser. But are they not groping towards a basic recognition of existing facts? Is there not something far more fundamental for society to recognize?

It will be admitted by all that physiological sex maturity is reached, by both male and female, some five years or more before our social development encourages and approves (with the blessing of Churches and State) marriage. Are we then to continue to erect artificial bans on natural and normal physiological processes, with all their strong urges? I am old enough to remember vividly farm life in remote Border farm "villages." Here it was a frequent, and not abnormal, occurrence for a girl of 16 to become pregnant by a lad of almost the same age. But the popular will and understanding, or "custom," was so strong that marriage always followed. The subsequent history of such couples compared favourably with those who entered first through church doors. In Lancashire also the old saying—"If thee houlds, lass, ald marry thee"—had much to commend it.

Is not the real solution for the State and the Churches to recognize basic physiological needs and attempt, at this level, to solve them? Even if in doing so they are

compelled to find a drug or injection that holds these impulses in abeyance.—I am, etc.,

Chipping Campden, Glos. C. B. HEALD.

SIR,—"The profession is not an arbiter of private morality," says Dr. B. S. Cooper (*Journal*, March 14, p. 715), who does not draw the obvious inference that doctors should not, at least corporately, act and speak as if they were experts in the matter. There lies the gravamen of the charge against the *Family Doctor* brochure as a whole, but other charges can be brought against individual articles. Thus, there is nothing in Dr. Eustace Chesser's article to indicate that his views are diametrically opposed to those of a very large number (probably the majority) of his colleagues, who would not agree that, as he appears to think, there is no more in marriage than four bare legs in a bed. ("We are made to believe that being in love, in other words being sexually attracted, is the one requisite for marriage.") Admittedly, he does say, "Nature has created a unity of our bodies and minds and society attempts to destroy this by working in exactly the opposite direction," but there he ends his pseudo-ethical teaching, whereas he might have followed Pascal, "Travaillons donc à bien penser: voilà le principe de la morale."

"Getting Married" could do much more harm than could the much-discussed *Lolita*, which makes no pretence of being a guide to behaviour (or to misbehaviour). Not only should the booklet be withdrawn: it should be disavowed by the Association as a whole.—I am, etc.,

London, W.1. A. PINEY.

SIR,—Modern society suffers from many ills. Not least of these is the "fig-leaf" delusion, which is to say that, if you do not look under the fig-leaf, there is nothing there. The ostrich-like attitude of a dissentient section of public opinion, be it medical, ecclesiastical, or civic, in coercing the B.M.A. to suspend publication of this ably presented and discreetly revealing booklet, does nothing to solve the problems of those about to be married.

Because one medical author asks if chastity is outmoded, or another states that one bride in eight is already pregnant, do their critics really suppose that these remarks are going to encourage immorality? On the contrary, by taking sex out of the cellar and attempting to deal with the problems that exist on a practical basis, people about to marry stand a better chance of adjusting themselves to the matrimonial state and its responsibilities as the result of reading these articles than they otherwise would.

I think it is a pity that the B.M.A., having set a wonderful example by producing a well-informed, well-written, and helpful, if at times frank, booklet of this nature, should bow to destructive criticism from sufferers of the "fig-leaf" delusion, no matter how sincere and well-intentioned their howls of abuse may be.—I am, etc.,

Bournemouth. GABRIEL V. JAFFÉ.

SIR,—I was shocked and horrified to hear of the withdrawal of the pamphlet "Getting Married." It seems incredible that our Association should commission a book, pass it as satisfactory, publish it, put it on sale, and then at the slightest outcry withdraw it. Whether Dr. Wand was *ultra vires* in doing so or not is beside the point. Its withdrawal was rank cowardice and a gross betrayal of the contributors. The time to have considered its desirability was when it was in the proof stage, not when it was on the book-stalls.

The main complaint seems to be that the articles by Drs. Eustace Chesser and Roger Pilkington made it clear that chastity is a vanishing quantity and that sex, whether premarital or not, is pleasurable. The former was pointed out by Terman many years ago, and he said that according to his calculations in a few years from now no girl getting married would be a virgin. The fact that sex is pleasurable is independent of morality. I have not always agreed with Dr. Chesser, but to my mind the fact that one does not concur with views makes it all the more important that they are not suppressed.

What can be the possible benefit of suppressing this pamphlet? Hiding the facts in a cowardly manner will not alter social *mores*. It has long been appreciated by those who have thought of the situation that safe birth control would finally lead to the disappearance of virginity. Does the B.M.A. now propose to abolish birth control? That would placate many of those whose disapproval it fears. Surely it is time that we acted as if we were grown up. A great deal of chastity has never been more than a myth, and to try to pretend otherwise will not alter reality. The best thing the Association can do is to face the facts and take the ban off this book.

I should be reluctant to resign after being a member for so many years, but it seems there may be no alternative if one wishes to retain one's respect for truth.—I am, etc.,

London, W.1. CLIFFORD ALLEN.

SIR,—I have read the current issue of "Getting Married" with great interest. I am a married woman doctor—the mother of a married woman doctor. I have been in general practice for 31 years and much of my work concerns marital problems. I consider this issue of "Getting Married" can do nothing but good, and I deplore its withdrawal from circulation, even temporarily.—I am, etc.,

Hampton, Middlesex. REBECCA DAVIS.

SIR,—As a doctor and a mother, I cannot see that Dr. Eustace Chesser's article in "Getting Married" could in any way corrupt. Whether or not I agree or disagree with what he has to say may be irrelevant, but what is relevant is that he should not be denied the right to say it.—I am, etc.,

London, W.1. HELEN BOWER ALCOCK.

SIR,—I have read the letters by Dr. George S. Turner, Dr. G. W. Piper, Dr. R. Preston Hendry, Dr. R. W. Cockshut, and Dr. R. W. Pinniger (*Journal*, March 14, pp. 714–715), and wish to say how strongly I agree with the opinions expressed.—I am, etc.,

Ashtead, Surrey. A. E. IRONSIDE.

SIR,—Dr. Eustace Chesser's opening statement of facts provides an answer to the question he poses: Is Chastity Outmoded? Following on, he endeavours to explain some of the factors underlying these figures—inherent, social, psychological, and/or lack of knowledge. He makes a plea for the spread of that tolerance which has been growing since the end of the Victorian era; he

expresses what in a democratic state must be a platitude, That the individual owes something to himself as well as to society. He does not advocate that chastity should be discarded but does think that the individual should be free to choose. His final creed is that the maternal instinct must in the end triumph, and, if not bedevilled and befogged by conventions, virtue will prevail.

The opening facts of the article are of course unpalatable, but they have to be swallowed and no amount of vituperation can alter them. If the figures are to be refuted then it must be by evidence not less convincing than that contained in the Chesser and Kinsey reports. Dr. Chesser was, I presume, invited to furnish this article, and, whether one agrees with it or not, one has no reason to doubt either his sincerity or his honesty, and the B.M.A. will do itself great discredit if it attempts to disown it.—I am, etc.,

Birmingham, 7. DANIEL T. GEMMELL.

SIR,—While in complete agreement with the views expressed by last week's correspondents (*Journal*, March 14, pp. 714 and 715) on the subject of the "Getting Married" booklet, even the title of which shows an absence of literary style, I feel that the fundamental point has not yet been mentioned.

To my mind, the most disturbing feature is the fact that a group of cranks and literary dunces were able to propound their eccentric views under the official auspices of the British Medical Association. While realizing that official comment must be postponed until after the next Council meeting, I think that the small annotation which appeared in your columns (p. 705) might have been more explicit about the "special powers" of the "special committee" set up in 1951 to produce *Family Doctor*. If the licence shown in the disputed articles is really permitted under these "special powers," then I feel that the Council must revise them, and must be more exacting in its future choice of personnel to serve on its "special committees." The Council cannot retain the respect of the members of the Association unless its standards are at least equivalent to theirs.—I am, etc.,

Glasgow, S.2. CONRAD J. SCHWARZ.

SIR,—We should indeed be grateful to Dr. S. Wand for having the courage to have "Getting Married" withdrawn from circulation. Much damage has already been done to the Association's good name by the publication of the booklet, but at least this gesture has done something to restore it. Christian morality is based not on an outmoded prudery but on the plain teaching of Our Lord, enshrined in the words "Holy Matrimony" of the marriage service.—I am, etc.,

Blandford, Dorset. CHARLES E. LANGLEY.

SIR,—The outcry over Dr. Eustace Chesser's article in "Getting Married" is yet another example of uneasiness about our own guilt and shortcomings. Every Christian (and I am one) believes in true chastity, but, as Dr. Chesser rightly says, "True chastity can only come from within ourselves, which means that it is we who must be free to make the choice." What good to anyone is chastity enforced from without? It may appease consciences, but it will not save souls. Dr. Chesser must have seen many patients who have tried to accept chastity with their minds but have failed to accept it with their hearts.

In my own experience I know how tragically parents (especially Christian parents) just do not face up to the problems of sex. Dr. Chesser had every right to say what he did. What is more, he said it extremely well and with obvious sincerity. I whole-heartedly support his article. Meanwhile, let those of us who call ourselves Christians put our house in order.

And would not this whole wretched business have been avoided had there been a note to the effect that the views expressed in "Getting Married" did not necessarily represent those of the British Medical Association?—I am, etc.,

London, S.W.1. RODNEY LONG.

Intermittent Suxamethonium Injections

SIR,—It is not generally known that the practice of using intermittent intravenous injection of the short-acting relaxant suxamethonium (succinylcholine) during anaesthesia is potentially dangerous.

My attention was drawn to this last year when I was invited to comment on a paper by H. V. Martin, of Germany, which was to be read at the International Symposium on Curare and Curare-like Drugs at Venice in September, 1958. (This paper and my commentary will be published shortly in the Proceedings with relevant references.) His findings, based on 114 cases with E.C.G. monitoring, and my own, based on over 100 cases, may be briefly summarized as follows:

(1) 15–30 seconds after the second and third injections of suxamethonium the heart rate suddenly slows to half or less of its former rate.

(2) The slowing usually lasts about 30 seconds: and is followed by a normal rate.

(3) Arrhythmia is common during the period of bradycardia.

(4) This effect occurs in about 80% females and about 60% males, being possibly less common in children.

(5) Cardiac arrest may occur for up to 16 seconds, or even longer, in 5–10% of cases, although the patient may not be paralysed at the time.

(6) The use of atropine as premedication, or intravenously before the suxamethonium, modifies the slowing effect and the arrhythmia, and reduces the incidence of both.

(7) The bradycardia occurs irrespective of the doses of suxamethonium used, from 10–200 mg.

(8) It occurs during the sequence thiopentone or hexobarbitone, followed by nitrous oxide–oxygen with or without trichlorethylene.

(9) The effect usually disappears after the third and subsequent injections.

(10) It is unconnected with spontaneous respiration.

(11) It is affected by artificial ventilation of the lungs by positive pressure.

This phenomenon is not to be confused with the bradycardia and/or hypertension which may follow a single injection, or accompany the use of a suxamethonium drip, both of which have been reported, the former being common in children. It may be deduced that the first injection sensitizes the heart in some way to the following two injections, and that the effect is thereafter lost.

Many anaesthetists are using this technique for operations like appendicectomy. Others may be interested in investigating the phenomenon. The following case should illustrate that it can be dangerous.

A female aged 64, blood pressure 240/125, weight 12 stone (76.2 kg.), was to undergo a vaginal operation. She received papaveretum gr. ¼ (22 mg.) and scopolamine gr. 1/150 (0.43 mg.) as premedication. Induction was with intravenous thiopentone 0.25 g., and a dose of suxamethonium (70 mg.) was given. Maintenance was

with nitrous oxide and oxygen (6/2 litres), semi-closed circuit, and trichlorethylene (about 0.7%) by face mask. Spontaneous breathing recommenced five minutes after induction. Eight minutes after the first injection of suxamethonium a second dose of 20 mg. was given intravenously. 25 seconds later the pulse abruptly ceased, spontaneous breathing still being present at the time. For the next two minutes a palpable pulse beat occurred only immediately following each occasion on which the lungs were inflated with the anaesthetic gases mixture (the trichlorethylene being turned off).

In view of this case, and two others in which cardiac arrest occurred for 7 and 10 seconds in a boy aged 10 and an adult female respectively, I now consider the method unsafe unless preceded by atropine at least gr. 1/100 (0.65 mg.) intravenously. Also it would seem that any further investigations would be better carried out in animals, until the whole matter is better understood.—I am, etc.,

Chislehurst, Kent. J. BULLOUGH.

Rubella in Pregnancy

SIR,—Dr. Noel H. Moynihan (*Journal*, February 28, p. 588) discussing a physician's opinion when consulted about termination of pregnancy after German measles, that "You can't do anything else,"[1] thinks "these simple words worth less than [the practitioner] imagined." The advice might be worth something if action had to be taken or if there was a choice of action, but as it stands it would be clearer with the addition "—or that either." However, the art of consultation may include diplomacy even approaching that of the Delphic oracle.

Considering that German measles epidemics vary very greatly, that they may include a number of quite different viruses, and that a 14-weeks foetus, as in this case, should be reasonably safe from eighth nerve damage, the whole incident is suggestive of throwing out the baby with the bathwater.—I am, etc.,

Wrose, Shipley. H. S. RUSSELL.

REFERENCE

[1] *Brit. med. J.*, 1958, **2**, 1349.

Patent Medicines on Television

SIR,—I am sure that countless numbers of my colleagues have sat, as I have, in silent, impotent rage whilst the television advertisements have poured out their nonsense exhorting the general public to buy a patent remedy. The appeal is to the most ignorant and least-informed section of the population at a time when they are presumably most susceptible because of dry irritating coughs or self-limiting influenzal types of illness. How one would like to be able to jump into the picture and shout out "Lies!", "Half truths!", "Don't believe it!", "Beware!". What satisfaction there would be from being able to debunk immediately the ultra-professional-looking gentleman of the advert and leave him deflated and defeated. Alas, this is not possible.

But are we quite as powerless to reply and to protect the public as we may think? If we look behind the new and unknown name of the manufacturer, may we not find an older and more familiar name of a firm active in the ethical market? And, if we cannot see this, perhaps a little market research by the B.M.A. might discover it for us. Perhaps then, as doctors, we might have a different attitude to the representatives and the products of firms we have hitherto only known through the glossy literature and blotting-paper they have sent us. The knowledge that the representative calling also represented a firm fanning the flames of public appetite for useless and perhaps sometimes dangerous patent medicines and happily exploiting this public addiction might well modify our approach, perhaps even ultimately prove a deterrent to these "non-ethical" activities.

By all means let us try to educate the public to be more self-reliant when faced with minor sickness, but not by encouraging the increased sales of "treatment" but by the realization that given a few days of rest at home most minor ailments cure themselves. There is a principle involved here which I feel we should realize even if others do not.—I am, etc.,

Liverpool, 8. C. TAYLOR.

Aspirin Plain and Buffered

SIR,—Your leading article (*Journal*, February 7, p. 349) provides an interesting review of the published papers on this topic. As I have pointed out (*Journal*, November 15, p. 1226), we can all draw our own conclusions as to the advisability of giving aspirin, in one or all forms, to an otherwise healthy person who seeks relief from minor pains. Whatever these conclusions are, it would certainly seem anomalous that preparations containing aspirin should be advertised to the general public for the relief of indigestion. We are told in the press, for instance, that "somebody's going to need 'alka-seltzer' for indigestion"; these tablets each contain 5 gr. (0.32 g.) of aspirin. Whether or not it is proved that aspirin can be dangerous for the healthy individual, I am sure that many doctors would not like to think that their dyspeptic patients were taking a preparation containing aspirin. Against this background, is it not wrong that preparations of the "alka-seltzer" type are advertised in this way?—I am, etc.,

London, S.E.1. JOHN DOBBING.

Student Suicides

SIR,—I read, with much interest, Sir Alan Rook's extremely lucid account of the above subject (*Journal*, March 7, p. 599), and also your leading article in the same issue (p. 633).

I think Sir Alan Rook clearly puts his finger on the main cause of the greatly increased suicide rate in Oxford and Cambridge, as contrasted with other universities, when he draws attention to the greatly increased percentage of residential students in the former, and suggests that "living at home has a stabilizing influence. . . ."

Mental breakdown in students does not differ fundamentally from that in any other section of the community, and therefore, with the exception perhaps of the somewhat rare case of schizophrenia, the immediate cause resolves itself into a question of the degree and duration of stress. All the stresses listed in this article and in your leading article—worry over work, examinations, strain of social adjustment, loneliness, sex difficulties, etc.—might well be found either alone or in combination in the breakdown of any young adult, and their elucidation, in my opinion, adds little or nothing to our understanding of this problem.

Primitive man realized that he had little hope of survival unless he could pass on his hunting skills to his sons. But in modern life the "skills of living" are assumed by parents to be effectively passed on to their sons in boarding schools and universities.

Stress is inevitable in all circumstances of life, but stress in the period under review (15–24) strikes the individual

when he is emotionally immature and especially vulnerable. The undue sensitiveness, undue suggestibility, poor sense of values, poor development of the necessary combative impulses (all signs of immaturity which the father, in more primitive times, would have speedily put right) of the average student make him, in many instances, peculiarly unfitted for the somewhat solitary, unguided life of the university. As a consequence, he is prone to many anxieties, to exaggeration of the trivial, and to be overawed very often by lectures and information much of which he will have to unlearn in later life. Apart from suicide, this immaturity, in my opinion, is also reflected in the high death rate by accident. Many of these deaths, I feel sure, could be ascribed to the taking of almost suicidal risks in mountaineering and with motor-cycles and motor-cars.

If figures were available, I think they would show a similar tragic state of affairs for young graduates, many of whom find, on leaving the university, that they are completely unfitted to cope with life with all its subtleties and perplexities and profound departure from the "picture" and the "ideals" they had formerly cherished.

There was no information in either Sir Alan Rook's article or in your leader on the influence of athletics, but I think students should keep in mind that bodily and mental activity draw energy from a common source, and that therefore a judicious balance should be struck.

Not, in my opinion, until universities (and boarding schools) pay as great attention to the complete maturation of the student as they now do to his intellectual equipment (and, in my opinion, this will necessarily include, for full maturation and stability, a coming to grips with spiritual issues) will there be any significant fall in the incidence of mental breakdown in students. Learning how to organize life, how to tackle difficulties, how much value to put on success (academic or otherwise), are all things which may, with difficulty, be learned by trial and error, but which it is much safer to learn from an intelligent parent or specially appointed adviser.—I am, etc.,

Pinner, Middlesex. ROBERT THOMPSON.

Achalasia of Cardia and Osteoarthropathy

SIR,—I was very interested to read the letter by Dr. J. Naish (*Journal*, February 7, p. 365) of a patient with achalasia who developed hypertrophic pulmonary osteoarthropathy as the result of a dilated oesophagus with secondary inflammation. There appear to be few references in the literature in which such an association is described. Be that as it may, I still consider that the development of clubbing, and more particularly hypertrophic pulmonary osteoarthropathy, in any patient with achalasia is an indication for a barium swallow and oesophagoscopy to exclude the possibility of a superimposed oesophageal carcinoma.—I am, etc.,

Charing Cross Hospital, London, W.C.2. M. A. PEYMAN.

Pseudomyxoma Peritonei

SIR,—Drs. C. F. Brennan, E. Fletcher, and Mr. J. Kyle in their interesting article on the diagnosis of pseudomyxoma peritonei (*Journal*, January 3, p. 27) say that work is now in progress to determine whether the mucus can be rendered more fluid by the administration of hormones and enzymes. This was so for enzymes in the following case, which, incidentally, satisfies closely most of the criteria set out by the authors.

In October, 1957, a 56-year-old housewife was admitted to hospital complaining of increasing abdominal distension and breathlessness for seven months. She had had ten children, and, apart from the ligation of her left internal saphenous vein in 1954 for varicose veins, had always enjoyed good health. Her enormous abdomen gave a fluid thrill, and shifting dullness was found. Rectally the pouch of Douglas was felt as a tender, fixed, lumpy mass which gave rise to the diagnosis of a generalized carcinomatosis. There were no other abnormal physical signs and examination of the blood, liver function tests, and radiography of the chest and abdomen gave no further information. Paracentesis at three sites with large cannulae produced on aspiration a thick, gelatinous, brownish, cloudy material, but no flow of fluid. Three days later I injected a total of 100,000 units of streptokinase and 25,000 units of streptodornase dissolved in 20 ml. of normal saline, about 4 ml. into each of five widely separated sites covering the abdomen. Next day a large trocar and cannula was inserted and 8 pints (4.5 litres) of semi-fluid, blood-stained material was obtained. Flow then eased, but when the cannula was removed after about 48 hours a total of 13 pints (7.4 litres) of fluid had been removed. Soon after the patient was discharged relieved.

Six months later she was readmitted with a recurrence of the ascites and examined by a colleague who found only gross ascites with a fluid thrill. Attempted aspiration, "abandoned, too gelatinous." Further streptokinase and streptodornase were injected intraperitoneally and more than 5 pints (2.8 litres) aspirated with a cannula connected to a pump. As the authors state, "It is the remarkable disparity between the healthy look in the patient's face and the seemingly hopeless findings in his abdomen which should suggest the correct diagnosis of pseudomyxoma peritonei." This patient had had her abdominal illness for a year, but was now described as "vivacious despite gross ascites," and the diagnosis was now made. This was confirmed at laparotomy by Mr. C. M. Craig, who found the abdomen "filled with quantities of gelatinous and pale semi-solid material, the whole of the serous surfaces plastered with an 'icing' material making all viscera unidentifiable. The pelvis was fused solid, but contained a multiloculated cyst one locule of which appeared to communicate with the peritoneal cavity. Quite impossible to recognize any anatomy or a line of cleavage—part of the cyst lining removed." Histologically this was shown to be fibromyxomatous and necrotic tissue.

The patient has been well since, and in the future a more concerted attack with enzymes may obviate the necessity of laparotomy.—I am, etc.,

London, W.2. M. R. MADIGAN.

Atony of the Female Bladder

SIR,—It seems possible that the aetiology of unexplained cases of "primary atony of the bladder" (*Journal*, January 17, p. 149) may be very simple—nothing more than habit. To avoid inconvenience, from a sense of personal cleanliness and from modesty, a perfectly normal growing girl may train herself to empty her bladder at longer and longer intervals until she has attained her object of having to pass water only twice in 24 hours, night and morning. Gradually, the dilating bladder becomes insensitive and she can continue her control without distress or even discomfort. An innocent habit, deliberate, due to ignorance of the physical effect. Obstruction diagnosed may be the result and not the cause.

I well remember, some 30 years ago, seeing post-mortem photographs in such a case. A young woman had so trained herself to the "night and morning only" habit, and died of an acute urinary infection. She had

an enormously dilated bladder, ureters the diameter of an ordinary lead pencil, and dilated pelves of the kidneys. There was nothing else amiss.

The condition is likely to continue to occur unless adolescents are taught the essentials of physiology and until not only public lavatories but also the toilets in offices and work premises are sufficient in number and are cleanly kept.—I am, etc.,

London, W.C.1. M. A. DOBBIN CRAWFORD.

Chloroquine in Rheumatoid Arthritis

SIR,—Your readers may have been left in some doubt as to the present status of chloroquine in the treatment of rheumatoid arthritis following the paper by Dr. H. Fuld and Dr. L. Horwich (*Journal*, November 15, p. 1199) and the subsequent correspondence (*Journal*, December 27, p. 1595, and January 24, p. 237).

To date there have been three reports of *short-term* controlled trials, my own[1] and that of Rinehart,[2 3] as quoted by Drs. Fuld and Horwich, and the third[4] from the Department of Medicine, Harvard Medical School. In each trial, distinct benefit has been demonstrated in the group treated with chloroquine compared with the control group. However, the maximum period of double-blind observation which served for this comparison was in my own trial and lasted sixteen weeks. All serious workers with chloroquine have noted that most cases relapse when treatment is discontinued as early as this. Unfortunately, the incidence of intolerable effects of the drug rises with continued therapy. The drug is either discontinued or the dose reduced to a level which might no longer be therapeutic. As a result, published figures of long-term uncontrolled trials give figures of 60–85% improvement, which are hardly better than figures published for simple treatment with aspirin.

The fact that a report of a *long-term controlled trial* of this drug has not yet appeared should not discredit chloroquine. This and related antimalarials may yet prove to be a valuable part of the growing armamentarium in the treatment of rheumatoid arthritis. Constant disparagement of endeavours in this field does more than discourage those who try. The impression is given that, because we cannot show with certainty any way of halting the rheumatoid process, then nothing at all can be done for the patient. Treatment by drugs, splinting, physiotherapy, and surgery is neglected, intermittent, or sought too late.

In recent years there has been a broadening in the description of the pathology and clinical course of rheumatoid arthritis and systemic lupus erythematosus which has served to blur the distinction between these two diagnoses. That chloroquine does something in lupus erythematosus is generally accepted. With this knowledge and the results of short-term trials in rheumatoid arthritis, I consider it reasonable to prescribe chloroquine for long periods in this condition. Perhaps chloroquine in rheumatoid arthritis should be regarded much the same as P.A.S. is in tuberculosis or perhaps penicillin in the prophylaxis of rheumatic fever. Rheumatoid activity will subside slowly, although periodic exacerbations are possible. Dr. A. L. Scherbel, of the Cleveland Clinic, Ohio, has told me that he prefers to regard chloroquine in rheumatoid arthritis much as we all do probenecid in gout; i.e., as an agent that will effectively but slowly reduce inflammation and the severity and frequency of recurrences. Doctors should also be mindful that rheumatoid arthritis damages the joints, and subsequent osteoarthritic degeneration can be inevitable. This degeneration will vary in severity and rate of progression from one patient to the next. Clinical manifestations of this degenerative process should not lead them to think that the chloroquine is not doing good.

My own method is to give chloroquine sulphate, 200 mg. twice daily (rarely three times a day initially). I may also give prednisone, 5 mg. twice or thrice a day in the first few weeks, tapering the dose off between the third and eighth weeks, during which time the patient's tissues become saturated with chloroquine. Prednisone may occasionally be needed for short periods subsequently, and in my experience infrequently. When secondary osteoarthritic weight-bearing joints are painful, I prescribe phenylbutazone (as well as giving advice on rest and arranging non-weight-bearing exercises). I try not to reduce the maintenance dose of chloroquine sulphate below 300 mg. daily: though some patients find benefit by 200 mg. daily, most do not. Treatment may have to be abandoned because of intolerable side-effects (giddiness, nausea, vomiting, pruritus, dermatitis, etc.), but these all subside within a week or two of cessation of administration. Other 4-aminoquinolines such as hydroxychloroquine sulphate and a diazanthracine are being tried as alternatives to chloroquine sulphate and chloroquine phosphate in the hope that they may have fewer side-effects.

May I also record the beginning of use of antimalarials in rheumatoid arthritis as I know it? Brennecke *et al.*[5] were the first to use primaquine and other 8-aminoquinolines, but toxicity was too great. They did not state their reasons for employing this group of compounds; possibly they knew of its value in experimental arthritis in rats which was reported by Kuzell *et al.*[6] Page[7] also in 1951 reported that among his patients with cutaneous lupus erythematosus treated with mepacrine two also showed an improvement in their accompanying arthritis. I then undertook a trial of mepacrine in rheumatoid arthritis, and this was published as a preliminary communication in 1952.[8] Mepacrine was soon replaced by chloroquines, as the former stained the skin and therefore could not be employed in a controlled trial. Happily, too, chloroquine is not dangerous, whereas prolonged use of mepacrine can be fatal.—I am, etc.,

Hackney Hospital, London, E.9. A. FREEDMAN.

REFERENCES

1. Freedman, A., *Ann. rheum. Dis.*, 1956, **15**, 251.
2. Rinehart, R. E., *Northw. Med. (Seattle)*, 1955, **54**, 713.
3. —— Rosenbaum, E. E., and Hopkins, C. E., ibid., 1957, **56**, 703.
4. Cohen, A. S., Calkins, E., *Arthr. and Rheum.*, 1958, **1**, 297.
5. Brennecke, F. E., Alving, A. S., Arnold, J., Bergenstal, D. M., and De Wind, L. T., *J. Lab. clin. Med.*, 1951, **38**, 795.
6. Kuzell, W. C., Gardner, G. M., Fairley, D. M., and Tripi, H. B., in *Rheumatic Diseases*, based on *Proc. Seventh Int. Congr. Rheum. Dis.*, 1952, p. 409. Saunders, Philadelphia.
7. Page, F., *Lancet*, 1951, **2**, 755.
8. Freedman, A., and Bach, F., ibid., 1952, **2**, 321.

Treatment of Coryza

SIR,—Allow me to break a lance with Dr. Thomas Parkinson (*Journal*, February 21, p. 496) about the use of preventive vaccines for colds. They are quite useless if given in the way he suggests, because a "cold" gives hardly any natural immunity. A susceptible subject can have a cold lasting three weeks and then catch another with only a few days clear in between. And that can go on all the winter. That sort of patient can be enormously improved by giving a small dose of anti-catarrhal vaccine every month from the beginning of September till the end of April.

I started using stock anticatarrhal vaccine in 1921 and am still getting it from the same maker, and I usually have half-a-dozen patients coming for injections every winter.

You may say that such cases should be fully investigated before submitting them to vaccine therapy. All right; and what happens then? You send them to a general physician, who sends them to an E.N.T. man, who gets the sinuses *x*-raved. The radiologist reports back to the E.N.T. man "sinuses clear"; the E.N.T. man sends the patient back to the physician, who returns him to the G.P., advising him to give him this or that nostrum the G.P. has not heard of

(I believe they have special blotters for consultants), and the G.P. is exactly where he started, having spent some £10 or £20 of the patient's or the State's money. And don't forget this, Mr. Consultant, we can't "murmur as we take our fees, there is no cure for this disease." We have got the patient "on our list" for the rest of time, and he, not unreasonably, expects us to do something for him.

For how many years should vaccine treatment be continued? For as long as the patient considers it necessary. The natural history of the disease is that people vary enormously in susceptibility, and the same person varies at different epochs of his life. On the whole children are much more prone to colds than adults, and old people are relatively immune. Anticatarrhal vaccine gives very pleasing results in children, only, of course, it takes a certain amount of parental determination to persevere with it. Of course, the treatment is not always successful; what treatment is? There are patients in whom vaccine fails altogether, and others who get perhaps two colds in a winter instead of about eight. I should consider that amount of relief worth while. If selected intelligently, I should say that 50 to 75% of patients benefit by anticatarrhal vaccine.

Lastly, let me say that I am really shocked that after nearly forty years absolutely no progress has been made in teaching students about the commonest malady they will meet in general practice. We richly deserve the layman's taunt, "You can't cure a cold, doctor."—I am, etc.,

Norwich. FREWEN MOOR.

Natural History of the Psychoneuroses

SIR,—In their discussion of the natural history of the psychoneuroses (*Journal*, January 17, p. 144) Dr. Harold E. R. Wallace and Miss Marion B. H. Whyte express some doubt about the adequacy of the data upon which, in an earlier paper,[1] I had based my observation that patients who did not reply to follow-up inquiries tended to fall mainly into certain distinct diagnostic categories—e.g., hysteria, alcoholism, and psychopathic personality. The complete data on the diagnostic distribution of discharges from the York Clinic for 1953 and three previous years were presented in a complementary paper elsewhere.[2] The 1953 figures, together with the diagnostic distribution of the non-replies, were as follows:

York Clinic: Diagnostic Distribution of Patients (1953)

International Code	Diagnosis	Number	%	Number Non-replies	%
301	Manic-depressive ..	131	40	5	21
311	Hysterical reaction ..	27	8	7	29
320	Pathological personality (includes addiction) ..	25	8	5	21
308	Organic psychosis ..	23	7	—	—
310	Anxiety reaction	22	7	—	—
302	Involut. melancholia ..	20	6	—	—
312/13	Obsessive-compulsive ..	16	5	1	4
300	Schizophrenia	16	5	1	4
322	Alcoholism	12	4	4	17
316/17	Neurosis with somatic symptoms	10	3	1	4
318	Hypochondriasis ..	8	2	—	—
303	Paranoia	7	2	—	—
304/5	Senile psychosis	4	1	—	—
325	Mental deficiency ..	3	1	—	—
328	Non-psychiatric	4	1	—	—
	Total	328	100	24	100

These figures, I think, will clear up any misapprehension which may have arisen from a reading of my original paper. Recent analysis of the follow-up findings for the year 1957 (335 discharges) points to the same conclusion. The largest single diagnostic category is manic-depressive illness (145 or 43%), followed by hysterical reaction (12%), schizophrenia (11%), anxiety reaction (7%), and others in diminishing proportion. Yet, of the 21 non-replies, 14 or two-thirds had a diagnosis of pathological personality, hysteria, alcoholism, or addiction. In other words, the share of these latter categories among the non-replies was 66%, although they represented only 21% of the total group.

There is, however, no reason to regard our two investigations as in any way comparable. To cite the main and most obvious difference, Dr. Wallace and Miss Whyte drew their sample exclusively from non-treated patients on a waiting-list (with the diagnostic classification arrived at from their reading of the notes), whereas mine covered fully investigated former in-patients, followed up one year after discharge.—I am, etc.,

York Clinic, Guy's Hospital, London, S.E.1. MOYA WOODSIDE, Research Psychiatric Social Worker.

REFERENCES

1 Woodside, M., *Ment. Hlth (Lond.)*, 1955, **14**, 58.
2 —— *Guy's Hosp. Gaz.*, 1955, **69**, 204.

Invalid Vaccination Certificates

SIR,—In your issue of March 7 (p. 644), Dr. I. J. Corbett, medical superintendent, Peninsular and Oriental Steam Navigation Company, referring to International Certificates of Vaccination or Revaccination against Smallpox, was not correct in saying that the necessary forms can be obtained from local public health authorities. These authorities do not keep them. They can, however, be obtained from all the main travel agencies or direct from the Ministry of Health in London or the Department of Health for Scotland in Edinburgh.

Perhaps I should add that it is the traveller himself who is expected to get the form and take it to the doctor. There is no obligation on the doctor, or a local authority or their medical officer of health, to supply these forms. —I am, etc.,

S. A. HEALD, Public Relations Officer, Ministry of Health.

London, W.1.

SIR,—The letter from the medical superintendent of the Peninsular and Oriental Steam Navigation Company (*Journal*, March 7, p. 644) rightly stresses the necessity for the correct completion of the "International Certificate of Vaccination or Revaccination Against Smallpox."

It would, however, be a pity if his complaint that "often no result is recorded" were to delay the issue of such a certificate to impending travellers abroad, because, when revaccination only is done, such recording of the result is unnecessary. It is necessary only in cases of primary vaccination, and, in fact, the official form provides no place for the certification of the result of a revaccination.—I am, etc.,

London, S.W.1. J. STUART HENSMAN.

Alcohol and Road Accidents

SIR,—The paper on the effect of small doses of alcohol, by Professor G. C. Drew, Dr. W. P. Colquhoun, and Miss H. Long (*Journal*, October 25, 1958, p. 993) deserves more attention than it has so far received here, though it has aroused much interest both in the U.S.A. and on the Continent. Professor Drew's investigations lasted some years and were again and again referred to in the long discussions of the Road Traffic Bill. The delay in their publication was made an excuse for not dealing with chemical tests in the Act of 1956.

Drew and his colleagues reached definite conclusions, which fully support the views of those who hold that

alcohol is a main cause of road accidents in spite of official figures to the contrary. Drew found that the level of alcohol in the blood is a fair indicator of the likelihood of an accident. Steering errors, particularly swings to the right, increase as soon as there is a measurable quantity of alcohol in the blood. He also found that short tests are unreliable, unless the deficiency is a gross one. These findings fully confirm the views of many, if not most, police surgeons. Policemen who have followed the zigzag course of a fuddled driver will recognize the pattern of driving. The largest dose given in these experiments was three pints (1.7 litres) of beer or five fluid ounces (142 ml.) of whisky, which raised the blood alcohol to 80 mg./100 ml.—less than that consumed by most offenders seen at police stations.

It is most important in the interests of road safety that these effects of slight intoxication should be realized. The majority of jury men and women are deplorably ignorant in this matter and unfitted to weigh up the clinical evidence impartially. That is why an objective chemical test should be legalized. Many medical men, and even police surgeons, have not yet read this very important paper, hence this letter.—I am, etc.,

Leicester. N. I. SPRIGGS.

Stiletto Heels

SIR,—Stiletto heels have been now fashionable for some time and they are being worn by a large number of people. The designers and inventors of these heels must have overlooked the serious injuries which they may inflict accidentally. The stiletto heel consists of a long narrow stem made of wood, but more often of aluminium. A round steel plate, one-quarter to five-sixteenths of an inch (6.5–8 mm.) in diameter, is screwed into the distal end of the heel, which is of the same diameter. After the shoe has been worn a little, the edge of the plate becomes serrated and in parts of razor-sharpness. The whole plate becomes like an inverted mushroom, broader at its base. The pressure exerted on the plate by a person of about 8 stone (51 kg.) in weight may reach about 1,800 lb. per square inch (126 kg. per sq. cm.). The wounds caused by such heels, when a person is accidentally trodden on or kicked by someone wearing them, can be very serious.

The following case illustrates this fully and shows the long invalidism which may result from such an injury.

A patient of mine, a schoolgirl aged 14, had her right foot trodden on while travelling in a bus on December 9. The injury was caused by a stiletto heel while its wearer was leaving the bus. The patient was seen the same day, when she had an irregular wound about 1 in. (2.5 cm.) in diameter on the dorsum of the foot about the middle of the shafts of the second and third metatarsals. Marked tenderness and swelling developed two days later and the girl was unable to use her foot. There were no signs of attempted healing on December 20, and the size of the wound was then 2 by 1.5 in. (5 by 3.75 cm.). After five days of parenteral penicillin the swelling and the tenderness began to subside. On January 7 the size of the wound was 1.25 in. (3.1 cm.) in diameter. The patient was then still walking with great difficulty, and this was over five weeks after the injury.

The girl was fortunate not to have the tendons on the dorsum of her foot severed, which could have easily happened in view of the enormous pressure that may be exerted by the worn end of a stiletto heel.—I am, etc.,

London, S.E.25. A. FRY.

Hula-hoop Syndrome

SIR,—Further to the letters by Dr. J. O. Newman and Dr. H. G. Nelson (*Journal*, December 20, p. 1531), may I record a most unusual sequel to the present fashion?

A Chinese female, aged 29, presented herself in the surgery with a history of persistent pain in the right iliac fossa, occurring immediately following vigorous exercise with a hoop two days previously. There was nothing else relevant to her symptomatology except that her last period 10 days previously was less profuse than normally.

On examination the patient was in obvious pain and tender in the right iliac fossa. Temperature and pulse were normal. On vaginal examination there was a tender lump in the right fornix and a smaller one in the left fornix. The patient was referred to Dr. Roddie in the Kandang Kerbau Hospital with a provisional diagnosis of torsion of the right ovary or an ectopic pregnancy.

On operation she was found to have a right-sided tubo-ovarian cyst bound down with numerous adhesions, which had undergone partial torsion, and a left similar but more mobile mass which was unaffected.

It thus appears that the hula-hoop has also entered into the field of medical diagnosis.—I am, etc.,

Singapore. F. B. E. KAMPFNER.

Surplus Beds and Nurses

SIR,—I was interested to read Mr. H. S. Shucksmith's comments on surplus beds and nurses (*Journal*, January 31, p. 300). With due respect to the admirable nursing service of this country I too feel that working hours of ward staff could be used with better advantage. I have seen much unnecessary energy (and tears) spent in preparing for doctors' and matrons' ward rounds, even to the extent of fluffing pillows and straightening blankets of sleeping patients in preparation for the night sister's round at 2 a.m.

Hospital routine in America is a less rigid and formal affair. The nursing service is admittedly lax; but this encourages the patient to help himself after an operation, resulting in a marked shortening of the time spent in hospital, with obvious benefit to patient and hospital authorities.—I am, etc.,

F. G. C. MEYNEN,
Medical Student.

The Royal Free Hospital School of Medicine,
London, W.C.1.

Catching up with Cabot

SIR,—Might it not be instructive if, in the cases discussed in your series of "Clinicopathological Conferences," the final diagnosis were given in the form of a correctly completed death certificate?—I am, etc.,

Department of Medical Statistics.
St. Bartholomew's Hospital,
London, E.C.1. M. P. CURWEN.

Epstein's Brain

SIR,—Sir Russell Brain's delightful reference (*Journal*, March 7, p. 643) to his bust by Sir Jacob Epstein reminded me of Shaw's remarks about his own bust by Rodin. "In years to come," said Shaw, "someone will ask: 'Who was Shaw?' and the reply will be: 'Un sujet de sculpture par Rodin, autrefois inconnu.'"—I am, etc.,

London, W.8. J. H. CARVER.

Obituary

W. CLARK SOUTER, M.D., D.O.

Dr. W. Clark Souter, the last of the older school of ophthalmologists in Aberdeen, died at Elgin on March 1 at the age of 79. He was one of a distinguished family of the sons of Alexander Souter. His elder brother, Alexander, was professor of humanity in the University of Aberdeen and a renowned classical scholar. His younger brother, John B. Souter, became well known as an artist and a portrait painter.

William Clark Souter was educated at Aberdeen Grammar School and at Aberdeen University, where he graduated M.B., Ch.B., with honours, in 1903. Taking an early interest in the physiological side of medicine, he studied the excretion of purine bodies, and for this work received his M.D., with honours, in 1906. Early after graduation, and at the request of Sir Alexander Ogston, he went as surgeon in the ship *Terra Nova*, which went to relieve the Scott expedition in the Antarctic in 1903–4. For this service he became one of the few to whom the Polar Medal has been awarded.

Dr. Souter's main interest was early directed to ophthalmology. He did postgraduate work at Moorfields and gained the Diploma in Ophthalmology of Oxford University in 1919. After further clinical experience at the Royal London Ophthalmic Hospital, he was appointed to the staff of the Aberdeen Royal Infirmary, and was associated with this institution until his retirement in 1946, when he was elected honorary consultant in ophthalmology. He was also surgeon to the Aberdeen Eye Institution and ophthalmic surgeon to the Aberdeen Maternity Hospital. The medical aspect of ophthalmology formed his most absorbing interest, and he followed all avenues of inquiry and research with scrupulous attention to detail. Verification of fact was the hallmark of his work, both in purely professional work and in his other intellectual activities. Among his publications were interesting papers on uveo-parotid fever and auto-eversion of the upper lids. In his long professional life he helped to train several generations of house-physicians and future ophthalmologists.

A member of the British Medical Association for 45 years, he acted as one of the honorary secretaries of the Section of Ophthalmology when the Association held its Annual Meeting at Aberdeen in 1914. He was a vice-president of the same Section at the Eastbourne Meeting in 1931, and president in 1939, again at Aberdeen. The B.M.A. awarded him the Middlemore Prize in 1917 and a scientific grant three years later. He was a pillar of support to the Aberdeen Medico-Chirurgical Society, hardly missing a meeting for the long period of 50 years. He was president of the society in 1932–3 and was elected an honorary member in 1958. His presidential address contained an echo of his Polar experience in making a study of the Eskimo kayak in the possession of the society and a comparison with examples in other museums. He also made a detailed study of the origins of the portrait of Harvey in the possession of the society and elicited the fact that Harvey visited Aberdeen on August 30, 1641, and was made an honorary burgess of the city. This portrait was mentioned in the study of the Harveian portraits made by Sir Geoffrey Keynes in 1949.

Crippling infirmity overtook Dr. Souter in his latter years, but until nearly the end he enjoyed a morning walk with his Cairn terrier, even in the worst weather. In one of his last walks he faced a blizzard and was assisted home by two Girl Guides, who were quite unaware of their help to an Antarctic explorer. His family mourn him—a son in medical practice in Northern Canada, a daughter in Australia, also a medical graduate, two daughters who took degrees in science, and his widow, who devoted herself to his care in the last days.—A. L.

I. E. J. THOMAS, M.D., M.R.C.O.G.

Mr. I. E. J. Thomas, consulting obstetrician and gynaecologist to the Pembury and Edenbridge hospitals, died at his home at Pembury, Kent, on February 23 after a long illness. He was 45 years of age.

Ivor Elwyn Joseph Thomas was born on November 8, 1913. Receiving his medical training at Guy's Hospital, he qualified in 1937, graduated M.B., B.S. in the following year, was elected to the membership of the Royal College of Obstetricians and Gynaecologists in 1940, and proceeded to the M.D. in 1941. After qualification he held the appointments of resident obstetrician at Guy's Hospital and tutor in the medical school. In 1939 he took up an appointment at Pembury Hospital, and continued to serve the hospital until his death, except for the period 1943–6, during which he served as a flight lieutenant in the R.A.F.V.R. during the second world war. He leaves a widow.

E. D. Y. G. writes: It was my great privilege to have known Ivor Thomas for very many years, and I counted him a friend and a colleague. His death at the early age of 45 has taken from the consulting staff of Pembury Hospital a young obstetrician and gynaecologist of great promise at the height of his career. He came to Pembury Hospital in 1939, where he had previously held an appointment with the Emergency Medical Service team from Guy's. He served with the R.A.F. in England and in France, and later returned to become gynaecological surgeon and then consulting surgeon to Pembury and Edenbridge hospitals, within the Tunbridge Wells Hospital Group. He was a careful and experienced surgeon, combining his undoubted operative skill with the knowledge acquired from wide reading and study of his specialty. As a teacher he was lucid and painstaking, and as a colleague universally popular. To his patients he was always courteous and considerate. In 1957 he first learned of the illness which in spite of extensive and continued treatment was to prove fatal so soon. During those trying months of intense pain and discomfort he showed a selfless courage and gallantry which were an inspiration to us all. We mourn the departure of a splendid and much-loved colleague, and our sympathy goes out to his widow in her sad bereavement.

WILLIAM KIRKWOOD, M.B., Ch.B.

Dr. William Kirkwood, who was in general practice at Weston-super-Mare for many years, died at Frenchay Hospital, Bristol, on February 21. He was 54 years of age.

William Kirkwood was born on October 12, 1904, and was educated at Glasgow University, where he graduated M.B., Ch.B. in 1927. After holding an appointment at Hawkhead Mental Hospital, near Glasgow, he entered general practice in 1928 at Cradley Heath, Staffordshire, but left there two years later to settle at Weston-super-Mare, where he remained until his death. He leaves a widow and one son.

K. C. M. writes: I had known Bill Kirkwood for the past 27 years, and it is a great blow to us all that he should have been taken so suddenly and so tragically from our midst. He was one of the best types of general medical practitioner and always had the interests of his patients at heart. He was ever ready to do his utmost for the sick and needy and was kindness itself in his attention to them. His cheerful disposition and sense of humour were an ever-welcome feature at any gathering which he attended, and his interests were many and varied, ranging from antiques to cricket. He had a lively brain and was vastly interested in everything that went on in the town of his adoption, being a very active member of the local medical association, the Somerset local medical practices committee, and also the local hospital management committee. His loss will be very keenly felt by everyone, but particularly by the writer, who was proud to be called one of his friends.

MARY F. WILLIAMS, M.B., D.P.H.

Dr. NORAH H. SCHUSTER writes: An old lady died on October 8, 1958, who was the recipient of the Ashanti medal for medical service with the Army just on sixty years ago. She was Mary Frances Williams (formerly Cornford), born in 1868, a daughter of the vicar of Horsley in Gloucestershire. She boasted an ancestry of intense nonconformity and martyrdom and she inherited in some degree the modern equivalents of her forebears. One of these had been burnt at the stake for his faith in the reign of Queen Mary, and two ladies by the name of Bruce on the other side of the family were bound and thrown to the rising sea-tide for refusing to submit to the Covenant. Mary Cornford's nonconformity began early with a refusal to learn to read till after she was 9 years old, but eventually she went to school in Clifton and on to Westfield College, London. She studied medicine at the Royal Free Hospital, where she obtained honours in physiology and a Helen Prideaux scholarship. She graduated M.B., B.S. (London) in 1897 and took the D.P.H. (Cambridge) in 1900.

While she was working for the D.P.H. at University College, she met Dr. Hamilton Williams, a son of Major General Thesiger Williams, and in 1898 they were married in Bristol by her father. Dr. Hamilton Williams had been in West Africa and Jamaica in the Colonial Service. Soon after their marriage they went to an appointment in Colorado, U.S.A., for a short time. Life was exciting and primitive, and Mrs. Williams freely indulged her talent with animals in her spare time. One of her pets was an irascible brown bear which mauled, and would have killed, a visitor if she had not interfered in time. In her old age she used to tell the story with relish.

In 1900 Dr. and Mrs. Williams were sent at short notice to Gambia to help with an epidemic of yellow fever. When this emergency was over they were both lent to the Ashanti Field Force "to afford assistance to the medical department," and were to be paid the same salary of £500 a year. Mrs. Williams was not put into uniform. Dr. Hamilton Williams is often mentioned in reports as having accompanied Army detachments on expeditions, but his wife gets little notice. Indeed, she appears anonymously in one personnel list as "a lady doctor" and in another as a nurse, so that it is impossible to follow her career with the Army. But she was probably working in hospitals at Kumasi and Cape Coast and together with her husband published some observations on cerebrospinal fever, which had been carried into that area by bearers from East Africa. Her services were recognized at the conclusion of this final Ashanti War, and she as well as her husband was awarded the medal in 1901.

They returned to England and settled in Birmingham for a time. In 1904 Mrs. Williams was appointed by the Worcestershire County Council to duties in connexion with the new Midwives Act. There was plenty of opportunity for her, since the midwives were deplorably untrained, and she did pioneer work for midwifery and infant welfare. About 1906 she started taking over the school work. The county council had introduced medical inspection before the 1907 Act, and Dr. Williams was active in the work. In 1908 she was made senior assistant medical officer for Worcestershire, and she claimed to have been one of the first school medical officers. An initial problem was the eradication of lice, and she had to endure some real persecution from parents who had always relied on lice as the outward and visible sign of health in their children. Opposition died down gradually, and with the support of the county council Dr. Williams ran an enterprising school service in those early days which included free milk, regular physical measurements, and care of mental defectives. One of the first open-air schools, founded by Miss Severn Burrow, was taken over by the council and also came under her care. In 1917 the Medical Women's Federation came into existence and Dr. Williams was one of the seven founders.

In 1933 she retired, and with her husband and son went to live in Bloxham, Oxfordshire, where she remained till her death in 1958. She very quickly endeared herself to the villagers by doctoring their pets, and at the age of 89 she still took a lively interest in any medical news, though disabled by ill-health and cataract.

Thanks are due to the Colonial Office for giving permission to the writer of this note to see papers from the Public Records Office, and to the librarians at the Royal Army Medical College, Millbank, and at the War Office for their assistance.

J. W. McINTOSH, M.B., B.Sc., F.R.C.S.Ed.

Dr. J. W. McIntosh, who was medical officer of health for King's Lynn, Norfolk, for over 20 years, died at an Edinburgh nursing-home on February 1. He was 83 years of age.

James Wilson McIntosh was born at Edinburgh on November 6, 1875, and was educated at the university there, graduating M.B., Ch.B. in 1897. Two years later he obtained the degree of B.Sc. in public health, and in 1910 was elected a Fellow of the Royal College of Surgeons of Edinburgh. After graduation he held the appointments of house-physician at the Royal Victoria Hospital, Edinburgh, and at the Edinburgh Fever Hospital, and clinical assistant at Edinburgh Royal Infirmary. Moving then to London, he worked as clinical assistant at the old City Orthopaedic Hospital and, later, as house-surgeon at the Royal Eye Hospital. During the first world war he served in the R.A.M.C., attaining the rank of major. After the war he became an assistant medical officer under the Durham County Council, his wife, Dr. Eleanor C. E. McIntosh, holding a similar appointment. They left Durham in 1927, moving to King's Lynn, where he was in general practice and also medical officer of health and school medical officer of the borough, and Dr. Eleanor McIntosh became honorary anaesthetist to the West Norfolk and King's Lynn Hospital. During the second world war his duties were greatly increased because King's Lynn was a reception centre for people evacuated from the larger towns. A member of the British Medical Association for 62 years, he was chairman of the West Norfolk Division in 1937–8 and president of the Norfolk Branch in 1947–8. He retired in 1948, and towards the end of his life he lived in Edinburgh.

M. C. writes: I knew Dr. J. W. McIntosh very well while he held office as medical officer of health for King's Lynn. As police surgeon at that time I frequently came in contact with him. Sometimes our problems were controversial and difficult, but owing to the sympathetic manner he had they were always smoothed out. He had an expert knowledge of all the difficulties he had to face, and always mastered them. He will be greatly missed, especially by the more humble and poorer members of the community, for in his private practice he enjoyed working for them. His real hobby was farming, and he used to derive much pleasure from his small farm just outside the borough.

R. L. WALKER, M.B., B.S.

Dr. R. L. Walker, a well-known general practitioner and former surgeon to the Lowestoft and North Suffolk Hospital, died at his home in Lowestoft on February 19. He was 62 years of age.

Robert Lawrence Walker was born, the son of a doctor, in Sandrakan, British North Borneo, in 1896. He was educated at Epsom College and St. Mary's Hospital, graduating M.B., B.S., London, in 1920. He served in the Royal Navy as surgeon-probationer from 1916 to 1918, and was house-surgeon and casualty house-surgeon at St. Mary's in 1918–19 before he qualified. After being in practice at Waltham Cross from 1921 until 1927, he moved to Lowestoft to join the late Dr. Muir Evans. He was

appointed surgeon to the Lowestoft Hospital in 1927, and held the post until he retired in 1949. During the second world war he was one of five or six doctors who remained in Lowestoft throughout this dangerous period in the town's history, working in the Emergency Medical Service as a surgeon, while at the same time conducting his own general practice and those of two of his colleagues who were serving in His Majesty's Forces. From 1949 until his serious illness in December, 1955, he continued to work at the hospital as supervisor of the casualty department.

Dr. Walker was chairman of the old North Suffolk Division of the British Medical Association from 1936 to 1939, and of the North-East Suffolk Division from 1939 to 1946. He also represented his Division at the Annual Meeting from 1941 to 1949 inclusive. He attained high rank in freemasonry, having held the offices of provincial senior grand warden of Suffolk and past assistant grand director of ceremonies of the Grand Lodge of England, as well as being a life governor of each of the Royal Masonic institutions and a vice-patron of the Royal Masonic Hospital. He leaves a widow, also a doctor, two sons, and two daughters.

S. B. H. writes: Lawrence Walker was the best type of doctor, possessing the invaluable gifts of kindness, consideration, and the capacity for taking infinite pains when confronted with a difficult medical or surgical problem. He was a capable surgeon, too, with sound judgment and a good pair of hands. Throughout our 21 years' association in general practice he always showed the greatest consideration towards me as his junior partner. When I had an opportunity about three years ago of applying for a less arduous post owing to ill-health, he put no obstacle in my way; indeed, he advised me to try for the job. At this time he was actually convalescing from a serious coronary thrombosis and his professional future was uncertain. Yet with characteristic unselfishness he put my welfare first. I shall always be grateful to him for his kindness to me. He will be missed greatly by his numerous friends and patients.

D. G. ROBERTSON, M.B., Ch.B.

Dr. D. G. Robertson died at his home at Seamill, Ayrshire, on February 21. He was 63 years of age.

Born on February 9, 1896, David Gordon Robertson was educated at George Watson's College and later at Edinburgh University, graduating M.B., Ch.B. in 1920. He then held the post of resident medical officer at the City Hospital for Infectious Diseases, Edinburgh. After a period of private practice in Polmont, Stirlingshire, he became a part-time medical officer at the local I.C.I. factory, later joining the company on a full-time basis. Subsequently he became divisional medical officer, Imperial Chemical Industries (Nobel Division), Stevenston. Dr. Robertson contributed to the discussions at many of the local meetings of the British Medical Association, speaking from a long experience of industrial medicine and of hazards to employees, and as an expert on this subject he will be greatly missed. He was an elder of the Barony church, West Kilbride. He leaves a widow, a son, and two daughters.—H. S.

PHILIP HAMILL, M.D., D.Sc., F.R.C.P.

The obituary of Dr. Philip Hamill was printed in the *Journal* of March 14 (p. 722).

J. C. N. writes: I should like to add the tribute of an old friend to what has been said about Dr. Philip Hamill. During the 'thirties I had the privilege of serving as his demonstrator in pharmacology and therapeutics at Bart's for some years. In later life, when I was appointed as surgeon to one of my present hospitals, I found him again, this time as senior physician. In a professional sense Dr. Hamill always seemed to be a combination of two distinct personalities. At Bart's and in his public work at the General Medical Council and elsewhere, he was very much the scientific man—essentially a physiologist with an incidental interest in the physiological action of chemical substances. His demonstrations at Bart's were mostly of a practical nature and consisted in mammalian demonstrations and classes run on the lines of physiological experiments. He had very little interest in teaching about the numerous drugs and their clinical application which were used in the medical practice of those days. He expected his demonstrator to deal with these details and other tiresome facts required by examiners. His principal objects were to teach students to observe facts and to draw their own conclusions for themselves. In the same way he appeared to care little for the traditional frills of prescribing, as evidence by his long fight in favour of the introduction of the metric system in medical practice. In these ways he seemed to be in marked contrast to my old professor at Oxford, Professor Gunn.

As a physician at the bedside Dr. Hamill gave a very different impression; no doubt the science was there all right, but to the patient, at any rate, he resembled one's conception of the best type of old-fashioned general practitioner. Large and impressive in manner, with a soft and comforting voice and gentle hands, he was a past-master in such important details as making the patient comfortable in bed, nursing care, and such questions as the food and drink (sometimes alcoholic) of the invalid. He was generally unwilling to submit sick patients to the numerous investigations, often of an unpleasant nature, so fashionable in scientific medicine to-day, although when he thought they might be useful he used them. In regard to surgery, when he considered that operative intervention was desirable there was nobody who could be more persistent in his persuasion of patient and surgeon alike. When he had succeeded in bringing them both to his view, he would take the trouble, as likely as not, to attend the operation himself.

I think perhaps, with his brilliant record, he may have been a little disappointed that he did not get on to the staff of his own hospital as a physician, but he was too philosophical and too sensible to mind very much. His death removes a colourful personality and a figure typical of an age which, alas, is rapidly disappearing. His friends and old pupils will hear of it with sorrow.

KATHLEEN M. WELDON BELL, M.B., B.S.

Mr. PATRICK CLARKE writes: I should be grateful if I could be permitted to add a few words to the obituary of Dr. Kathleen Bell which appeared in the *Journal* of February 21 (p. 514). As senior anaesthetist to the regional neurosurgical centre at Newcastle she naturally came in contact with very many young people in training and with visitors to the unit. To all of these she extended a wonderful hospitality, completely natural and making every stranger feel that he or she was "one of the family." There must be many who remember with gratitude days spent at her country home at Ovington in Northumberland, where she loved to receive visitors in her large garden and to share with them the wonderful view over the valley of the Tyne. For her, honesty was not merely the best policy—it was the only one; and by her example she must have influenced many. Some five years ago she had a dangerous illness which would have deterred most from continuing, but courageously she returned to full duties, taking her full part in both emergency and routine work. Whether she was anaesthetizing for a senior colleague or for the most junior trainee her demeanour was exactly the same, courteous and helpful. She died in the ward where she had worked, and no one who was there at the time of her last illness is likely to forget the deep and obvious sorrow of the staff. She was the friend of all.

N. W. writes: I would like to add a small tribute to the memory of my old friend, Dr. Kathleen Bell. For almost 10 years we worked together in the neurosurgical theatre of the Newcastle upon Tyne General Hospital. Her presence, charm, and extreme capability made her a great favourite

with all members of the staff; she was a most valued member of the neurosurgical team. The last time I saw her was on July 30, 1955, immediately before my departure for Scandinavia. My wife and I dined with her at Ovington. As we finished, the telephone rang asking her assistance in a car accident on the main Newcastle–Carlisle road, which ran near by. We went out together and rendered what little aid we could to three or four injured people and arranged their transport to Hexham Hospital. It transpired afterwards that she was frequently asked to do this sort of thing, and the ambulance people knew they could always depend on her help. Nothing, day or night, was ever too much trouble for her. Although she was well aware of her illness and its possible complications, she never spared herself; she had tremendous courage. Newcastle has produced several great women doctors in the past and Kathleen Bell is assured of a place in their ranks. She will long be remembered by all her friends.

Sir PERCIVAL NICHOLLS, K.C.B., F.R.C.S.

The obituary of Sir Percival Nicholls was printed in the *Journal* of March 14 (p. 722).

J. A. M. writes: Many will have read with regret of the death of Sir "Percy" Nicholls. Good doctor, athlete, and shipmate, he was genuinely fond of the Navy, and happy in his naval life. Serene and shrewd, he was a wise and kindly adviser to his juniors, whom he supported staunchly. The writer spent under his command some of his happiest naval years, and with many others will feel deep sympathy with his family.

R. SESSIONS HODGE, M.R.C.S., L.R.C.P., D.P.M.

The obituary of Dr. R. Sessions Hodge was printed in the *Journal* of February 14 (p. 443).

F. B. writes: Rae Hodge enjoyed fast cars and was a very fine driver. He maintained a very high average speed throughout his life, and, as others have already written, covered more ground in his time than most of us could hope to do in twice the years. Colour-blind, as many members of Quaker families are, he was compensated by an extraordinarily accurate ear, was an excellent mimic, and enlivened many a case conference by reporting the *ipsissima verba* of his clients in dialect. His contributions to medicine were many, and noteworthy were his papers on the use of stilboestrol in controlling libido and (with Professor F. L. Golla) on the value of acetazolamide in epilepsy. Co-opted to the joint committee of the British Medical Association and the Magistrates' Association, his wide medico-legal experience contributed greatly to the recent memorandum on the law and practice in relation to attempted suicide in England and Wales. He made himself a master of the difficult technique of electroencephalography, and many members will recall his superb demonstration of a pykoleptic boy by a simultaneous film, sound track, and E.E.G. recording at a B.M.A. scientific meeting.

W. J. STUART, C.B.E., M.B., F.R.C.S.Ed.

The obituary of Mr. W. J. Stuart was printed in the *Journal* of March 7 (p. 652).

D. A. H. writes: Allow me to write a few words of appreciation of the late Mr. W. J. Stuart, honorary consultant surgeon to the Edinburgh Royal Infirmary, who died on February 23 last. To doctor and student he was always affectionately known as "Pussy" Stuart. The following incident will reveal his true character. On one occasion he was asked for his opinion on an abdominal case by one of the honorary consultant physicians. After a lengthy bedside discourse the physician callously remarked, "I think you had better open him up and look inside." Mr. Stuart was quick to see the distress caused by these unkind words. He quietly stepped forward and knelt at the side of the patient's bed and spoke a few words to him, and the patient's face immediately became radiant and happy.

Medical Notes in Parliament

HEALTH SERVICE EXPENDITURE

When the Supplementary Estimate of £16,589,706 for the Health Service was presented to the House of Commons for approval on March 12, the Minister, Mr. D. WALKER-SMITH, described it as no more than the best estimate that could be made in January. Because of the difficulties of predicting so much of the expenditure they could not even now be certain that it forecast within narrow limits the expenditure that would in due course be shown to have been incurred.

A Rise of 3½%

The amount of the estimate was an increase of 3½% on the original estimate for the year of £472,459,430. Its four main items were hospital revenue, general medical services, pharmaceutical services, and poliomyelitis vaccine. For hospitals, the original estimate of £354,566,000 had been increased by £8,700,000. A large proportion of this expenditure was on salaries and wages. The £8,700,000 was made up of Whitley awards, £3,500,000; price increases, £500,000; acceleration of maintenance work and replacement of equipment, £4,600,000; and plant replacement, £100,000. The increases for wages and prices, together £4m., compared with increases of £8m. for the same items in the last financial year, and of £13m. in 1956–7. The Whitley item included the award of £1,626,000 for domestic and ancillary staffs; £927,000 for the regrading of administrative and clerical staffs; and £325,000 for medical and dental staffs.

The £2,200,000 for general medical services arose from two main causes—the advance payment on account of the balance of the central pool for 1957–8; and the money paid on account of the further interim increase of 4% to general practitioners with effect from January 1.

The £2,200,000 now being provided for the pharmaceutical services brought the total cost to £69m.—a large amount, but only about one-tenth of the revised estimate of £675m. for the total cost of the Health Service in England and Wales this year.

Prescribing Costs

The expectation in the original estimate was that there would be about 216m. prescriptions at an average cost of 6s. each. The revised estimate was fewer prescriptions at a higher cost—205m., at 6s. 5½d. each. The charge of 1s. an item instead of 1s. a form introduced in December, 1956, had the result that some doctors prescribed larger quantities at less frequent intervals. Then a corrective influence came on the scene, in the Asian flu epidemic of autumn, 1957, which had the reverse effect, increasing the number of prescriptions and reducing the cost.

The reasons for the increased expenditure were, first, the general upward trend of costs; and, second, the introduction of new drugs and preparations. The newer drugs—for example, antibiotics, corticosteroids, and certain cardiac preparations—now accounted for about 40% of the total ingredient cost of prescriptions. One single new drug introduced early this year which was of particular value in the treatment of elderly patients might now be costing £1m. a year. The cost of these new drugs must be balanced against their value to the community, medically, and also indirectly by shortening illness and promoting a speedier return to work. The pharmaceutical industry had considerable achievements to its credit for which the nation should be grateful. The tendency to prescribing larger quantities, which was not necessarily uneconomic—in chronic illness it was a perfectly proper practice—did not seem to have gone significantly further since 1957.

Agreement with Pharmaceutical Industry

The agreement negotiated with the drug industry about the prices of most proprietary preparations was more than

half-way through the trial period. They were watching its progress very closely "in the context of what the position will be and what it should be at the end of the trial period." At the same time they were doing all they could to encourage economy in prescribing. He was adopting the Hinchliffe Committee's recommendations in their interim report designed to secure that fuller information is put in the hands of doctors to help them in discharging this duty. He was looking forward to receiving the committee's final report, perhaps next month, and would at once give careful and constructive consideration to its further suggestions.

Polio Vaccine

The last main item was the £1m. for the purchase of poliomyelitis vaccine. Considerable strides had been made with the immunization programme. At the end of 1958 over 6m. children had been vaccinated twice, and nearly 250,000 were awaiting the second injection. Over 750,000 had received a third injection under the expanded programme announced last July. There was plenty of vaccine available for late registrants, and parents who had failed to register their children should not delay longer if they wanted to ensure vaccination before the next poliomyelitis season.

Unfortunately young adults, the 15–25 age group, who were also included in the extended programme, had been dragging their feet. They should come forward at once in their own interests. The incidence in this age group was not as high as with the younger children, but for those who did contract it at that age the severity and the degree of paralysis were much greater. He had sent letters to local health authorities making suggestions about arrangements that might help to improve the response of this age group.

Debate on the Estimates

The debate which followed was largely concerned with the cost of drugs. Dr. EDITH SUMMERSKILL (Warrington, Lab.), denying any pleasure in saying "I told you so," covered the familiar ground that the Government had been warned of the likely results of the 1s. per item charge and quoted the B.M.A. as saying, "The composite packs of medical supplies which the Minister said he would introduce and save a shilling or two was not the answer. The B.M.A. warned them that it would create wastage. A further result would be a tendency to over-prescribe which might result in waste and more expense to the Service than ever before," and added the comment, "I have never before said in the House that the British Medical Association was absolutely vindicated."

She also asked if hospital prescribing was subject to the same scrutiny as that of the general practitioner, and what treatment was meted out to specialists who were known to favour always the latest proprietary drugs. On new drugs and preparations she repeated the accusations of over-charging by American firms, using as an illustration the cortcosteroids which, after being said by the Minister to be fair and reasonable, were reduced in one instance from £56 to £12 per 1,000 tablets.

"Ring of Producers" Blamed

Mr. M. EDELMAN (Coventry, North, Lab.) took the argument further. He had felt when reading the report of the Public Accounts Committee for 1956–7 that the whole onus of cutting down the cost of the pharmaceutical service was being laid on the doctors. Far from the doctors being at fault, the actual responsibility—particularly in proprietary medicines—lay in the fact that these drugs had fallen into the hands of a ring of producers which was demanding from the public prices that, if translated into terms of other products, would cause a tremendous wave of protest. The proof that there was exploitation of the sick by a price ring lay in the way that the biggest customer in the world, the Health Service, had necessarily to pay more and more for its pharmaceutical products.

Dr. DONALD JOHNSON (Carlisle, Con.) thought that one of the most disturbing figures disclosed in the hospital costing returns was the estimation of the cost of out-patients, which worked out at about 17s. 6d. per attendance, almost as much as a Health Service doctor got for attending the patient throughout the whole year. Too many trivial and minor cases were sent to out-patient departments. He put in a plea for the old-fashioned simple remedies, and questioned the habit of thinking that because drugs were expensive they must be effective.

"B.N.F." Applauded

Sir HUGH LINSTEAD (Putney, Con.) said that few industries were more closely under financial scrutiny than the pharmaceutical industry. Less than justice had been done to the Ministry of Health, the B.M.A., and the Pharmaceutical Society for the publication of the *British National Formulary*, which had had a remarkable effect in keeping down the cost of drugs. In Canada and the U.S. about 90% of the prescriptions were proprietary medicines, whereas in this country the figure was about 50%. That was largely due to the publication of the *National Formulary* as a guide to prescribing. He thought a solution to the shortage of pharmacists in hospitals and the unbalanced nature of the service might be found in the creation of a group pharmaceutical service.

Mr. DENIS HOWELL (Birmingham, All Saints, Lab.) voiced the objections of the Labour Party to private patients having free drugs, which would lead, in his opinion, to an increase in their numbers and then to demands for preferential treatment. He also expressed concern about the trend for consultants to change from full-time to maximum part-time service. It was linked with the question of pay-beds, in which there had been a "terrific" increase. The system of merit awards should be carefully examined. It was the only branch of public expenditure in which money was paid out in an atmosphere of secrecy.

Government Reply

Mr. RICHARD THOMPSON, the Parliamentary Secretary, replying to the debate, told Dr. Summerskill that seven of the ten Hinchliffe recommendations had been accepted completely or substantially, one had been referred to the Royal Commission on remuneration, and two were being discussed further by the committee and the Pharmacopoeia Commission. The question of consultants had been the subject of evidence given to the Royal Commission on remuneration, whose report must be awaited. He detailed the methods in use or under contemplation to make doctors and hospitals cost-conscious about drugs and medicines.

The original estimate plus the supplementary provided £2.7m. for poliomyelitis vaccine, about £900,000 of it for British vaccine, and £1.8m. for American and Canadian. The price being paid for British vaccine at present was substantially higher than the recent prices for American and Canadian vaccine. The quotations were not identical from the three American firms from which it was bought. British supplies last year were nothing like as much as the Ministry would have wished to purchase, so they were buying relatively small quantities, and again the prices were not uniform.

Price Regulation

Mecamylamine was now made here by a British-based subsidiary of the U.S. firm. A patent had been applied for, and if granted it would run for 16 years, and the drug would be available in proprietary form only from the manufacturers or anyone who had a licence to manufacture. The Controller of Patents could order a licence to be granted on terms which sought to secure that the medicine should be available to the public at the lowest prices consistent with the patentee's deriving a reasonable advantage from his patent rights.

The voluntary price regulation scheme agreed between the Health Departments and the Association of British Pharmaceutical Industry applied in practice to roughly

60% by value of all proprietaries. Before its expiry in June, 1960, its working would be reviewed in all aspects, to see whether the scheme should be renewed, whether it needed to be improved, or what should be done. It was unrealistic in calculating profit figures to take the raw material cost, compare it with the price of the finished product, and call the difference gross profit. He concluded with the announcement that Sir Ewart Smith had agreed to serve as chairman of the council which the Minister was setting up to assist in the development of efficient techniques in the Health Service. The names of the other members would be announced shortly.

Supplementary Estimates Agreed

The Estimate, and a corresponding Supplementary Estimate of £2,376,500 for Scotland, were agreed to.

MENTAL HEALTH BILL

What are generally called the censorship powers in the Mental Health Bill remain unchanged—except for a promised addition to meet a point made by Dr. EDITH SUMMERSKILL—after a wide discussion by the Standing Committee on March 10. They were criticized on grounds both of principle and practice by Mr. KENNETH ROBINSON (St. Pancras North, Lab.), but in a vote on his proposal to delete subsection (2), relating to outgoing mail from patients, he mustered only three other supporters, and found 26 against him.

Censorship of Outgoing Mail

Dr. SUMMERSKILL (Warrington, Lab.) offered a new definition for letters that should be withheld from dispatch. That in subsection (2) uses the words "unreasonably offensive to the addressee." The words she proposed were "contains libellous matter concerning third parties, other than hospital staff, or information which may be detrimental to the patient." She was anxious to protect the patient against himself. The subsection as drafted protected only the addressee. Defamatory letters might be written while a patient was in hospital suffering from mental disorder. There would come a time when the patient returned to his home as a normal man, and might be shown the letters he had written.

She explained that "libellous" was used not from any apprehension that patients might have to be protected against actions for libel, but to illustrate the form of defamation that might be conveyed in a letter. The MINISTER OF HEALTH viewed the suggestion as an improvement, and agreed that protection should be extended to save the patient from his own detriment. He preferred the word "offensive" in regard to the addressee, while "libellous" might be the better word in regard to third parties. He undertook to put the subsection in order for the report stage of the Bill, and indicated that this would probably be by a blending of the present drafting and the amendment. On this assurance the amendment was withdrawn.

Another amendment, moved by the Minister, to include among those from whom letters should not be withheld the Deputy Master of the Court of Protection and subordinate officials, was agreed to. The Bill as drawn mentions only the Master of the Court.

Leave of Absence from Hospital

At the meeting of the committee on March 12, Mr. K. ROBINSON had the support of Dr. SUMMERSKILL for a proposed change in Clause 29 (leave of absence from hospital) to extend from six to 12 months the period of leave of absence for a patient. There was on the whole, he said, no real objection to the six-months period for mentally ill persons, but for mental defectives it was too short. The amendment was supported by the Society of Mental Welfare Officers, the Royal Medico-Psychological Association, and the National Association for Mental Health. He had also received representations from people who employed mental defectives on licence. The argument was that, while many patients would be perfectly all right for several months, they might break down when the pressure of community life and the change from institutional care had a cumulative effect and need further treatment and training. There was also some fear that the limitation might result in a "cat and mouse" process, and an almost automatic recall at the end of six months to be on the safe side. It was generally thought that 12 months would produce the best results all round.

Mr. D. WALKER-SMITH pointed out that the six-months leave had two effects: it made the power to recall a patient lapse; and it made the authority for detention lapse unless it was transferred within the period to guardianship. It was founded on the considered view of the Royal Commission. Six months, he emphasized, was not the period within which a final decision had to be taken on whether the patient should return to hospital. It was only the period in which arbitrary recall was possible. At the end of the six months the patient need not be discharged from all care and control, because he could be transferred to guardianship—for example, of the local health authority—even before the period lapsed.

While the patient was on leave of absence from hospital he would normally be supervised from the hospital; but when he had been in the community for a reasonable length of time, the principle being followed in the Bill suggested that it was right for him to be supervised, not institutionally, but by the local health authority, who were basically responsible for care and aftercare. Under the amendment the licence period with the arbitrary recall would go on for 12 months. The clause provided the more liberal procedure of the two, because the arbitrary recall went at the end of six months, and it was quite possible, if the patient was then ready for it, for him to go into family life straight away.

The amendment was withdrawn, but not until Mr. ROBINSON had entered the objections that the local authority services did not yet exist in many areas, and that if those who worked in mental hospitals did not agree with the Bill they would adopt the cat-and-mouse procedure of recall at the end of 5½ months in the interest of the patient as they understood it.

QUESTIONS IN THE COMMONS

General Practitioner Service

Sir MALCOLM STODDART-SCOTT (Ripon, Con.) asked the Minister of Health on March 9 what percentage of the population in England and Wales were not on doctors' lists and did not use the free practitioner service; and by how much this percentage had increased or diminished during recent years. Mr. WALKER-SMITH: Exact information is not available, but it has been estimated that this percentage is of the order of 3%. I have no reason to think that it has changed much over recent years.

Vacant Medical Posts in B.W.I.

Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) asked the Secretary of State for the Colonies what medical posts in the British West Indies calling for recruitment from Great Britain remained unfilled at the latest available date.

Mr. J. AMERY, Under Secretary, stated on March 10 that vacancies numbered 32, and 6 candidates had so far been selected against them. The vacancies were:—*Barbados:* 1 assistant radiologist, 2 medical officers of health, and 1 registrar (medical). *British Guiana:* 1 pathologist, 1 medical superintendent for a mental hospital, 1 obstetrician and gynaecologist, and 1 surgeon. *British Honduras:* 2 medical officers. *Jamaica:* 1 surgeon, 1 bacteriologist, 1 assistant bacteriologist, and 4 medical officers. *Leewards:* 1 medical officer. *Trinidad:* 4 medical officers (Grade C), 4 medical officers (Grade B), 1 pathologist, and 1 medical officer of health (Grade A). *Windwards:* 4 medical officers.

Tuberculosis in Hong Kong and Singapore

Mr. S. AWBERY (Bristol, Central, Lab.) asked what percentage of people in Hong Kong and Singapore were suffering from tuberculosis; what was the death rate; and, in view of the satisfactory methods of dealing with this disease in the United Kingdom, what steps were being taken to introduce similar remedial measures in the two colonies.

Mr. AMERY replied that in Hong Kong 2% of adults had the disease in active form. The death rate in 1958 was 83.8 per 100,000. In Singapore there was no accurate figure available for the whole population. Preliminary results of a case-finding programme conducted last year among those over 14 years of age showed that, of those *x*-rayed, the percentage suffering from the disease in its active form varied from 1.1 in the rural area to 4.7 in the city area. The death rate in 1957 was 51 per 100,000. In both places vigorous campaigns were being waged against the disease, and in both all proved remedial measures employed in the United Kingdom were already applied. To Mr. AWBERY's comment that the incidence in Hong Kong and Singapore was the highest in the world and cried aloud for more to be done to reduce it, Mr. AMERY replied that the death rate in Hong Kong in 1958 was the lowest on record, and that in Singapore the death rate had fallen from 117 per 100,000 in 1950 to 51 in 1957–8.

Misleading Advertisements on T.V.

Sir LESLIE PLUMMER (Deptford, Lab.) asked the Postmaster-General on March 11 whether, in view of complaints by professional bodies and individuals that advertisers are making extravagant claims for their products on Independent Television, he would make regulations under Sections 4 (4) and 4 (5) of the Television Act that any such claim must be capable of proof and demonstration before an independent committee. Mr. ERNEST MARPLES: One of the functions of the Authority's Advertising Advisory Committee is to give advice to the Authority and programme contractors with a view to the exclusion of misleading advertisements. Such advice has been given and acted upon. I see no need therefore for regulations by me under Section 4 (4) or directions under Section 4 (5).

Sir LESLIE PLUMMER asked if the Postmaster-General was aware that, when his predecessor announced the setting up of the Advertising Advisory Committee, he had allayed the fears of a large number of Members as to whether exaggerated claims would be made. Now, demonstrably, exaggerated claims were being made, so would he now look at the constitution of the Advertising Advisory Committee to see whether it was advisable to have representatives of advertising agents on it? Mr. MARPLES replied that he was satisfied with the composition of the Advertising Advisory Committee, which was a responsible body of experts drawn from all spheres of life. The British Medical Association, the Pharmaceutical Society of Great Britain, the Ministry of Health, and the veterinary surgeons all were represented on this body. He was certain that they were expert and efficient. If Sir Leslie had any specific exaggerations in mind he would refer them to the Advertising Advisory Committee.

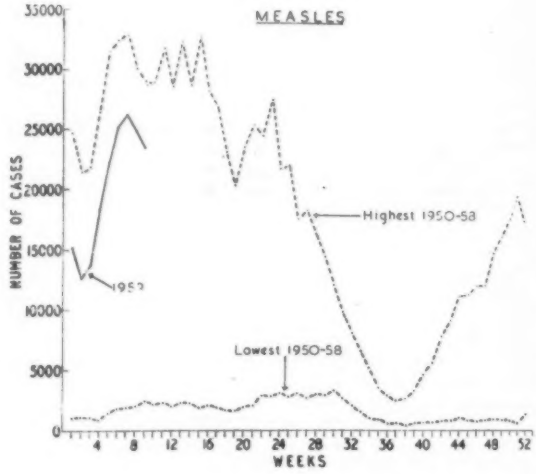
Factory Inspectorate

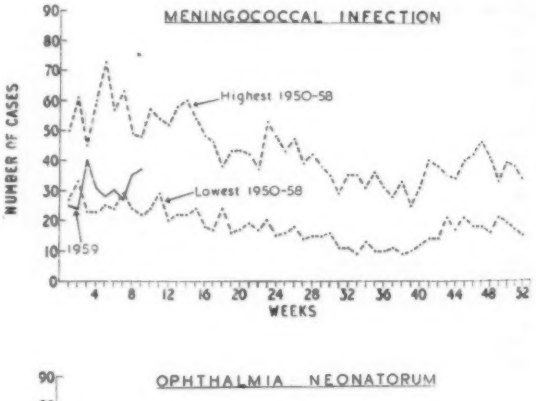
Dr. B. STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Labour whether the Departmental Committee appointed by him in March, 1957, to inquire into the duties, organization, and staffing of the Medical Branch of the Factory Inspectorate had yet reported; and when it was proposed that the report shall be published. Mr. IAIN MACLEOD: The committee has reported. I propose to publish at an early date the results of the committee's survey and the decisions I have reached on the points raised.

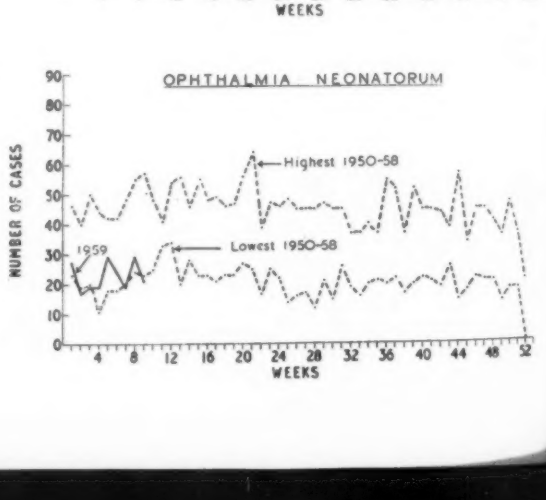
Vital Statistics

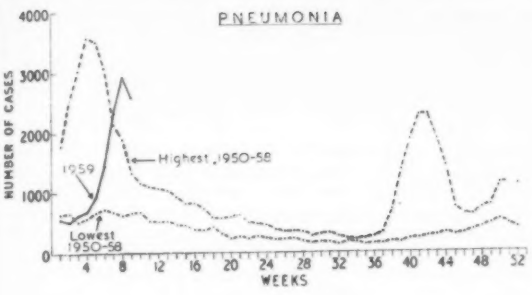
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ------, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending March 7

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available:

	Week Ending Feb. 28	Week Ending Mar. 7
Measles		
Essex	2,423	**2,286**
Ilford M.B.	257	**223**
Hornchurch U.D.	253	**182**
Romford M.B.	251	**153**
Lancashire	2,134	**1,887**
Liverpool C.B.	252	**165**
Manchester C.B.	224	**315**
Preston C.B.	205	**62**
London	1,419	**1,360**
Wandsworth	160	**152**
Northumberland	365	**423**
Newcastle upon Tyne C.B.	225	**278**
Staffordshire	840	**743**
Stoke on Trent C.B.	191	**180**
Warwickshire	1,531	**1,337**
Birmingham C.B.	647	**582**
Coventry C.B.	351	**347**
Yorkshire West Riding	2,601	**2,533**
Bradford C.B.	267	**287**
Leeds C.B.	485	**453**
Sheffield C.B.	326	**380**
Harrogate M.B.	164	**138**
Glamorganshire	393	**463**
Cardiff C.B.	156	**250**
Dysentery		
Glamorganshire	118	**112**
Cardiff C.B.	59	**60**
Barry M.B.	26	**10**
Rhondda M.B.	22	**22**
Lincolnshire	158	**118**
Grimsby C.B.	82	**49**
Boston M.B.	14	**8**
Cleethorpes M.B.	15	**12**
Warwickshire	87	**71**
Coventry C.B.	62	**47**
Acute Poliomyelitis		
Hampshire	2	**4**
New Forest R.D.	1	**3**

4 of the 6 cases of paratyphoid fever were notified in Middlesex.

All the 9 cases of acute poliomyelitis were paralytic, and compared with the preceding week the cases were 2 more for paralytic and 2 fewer for non-paralytic cases.

No further cases of smallpox have been notified at Liverpool beyond the 1 mild case reported last week (*Journal*, March 14, p. 731).

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 28** (No. 8) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959 Eng. & Wales	1959 Lond.	1959 Scot.	1959 N. Ire.	1959 Eire	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire
Diphtheria	5	0	4	0	3	6	1	4	0	1
Dysentery	1,049	67	122	14	8	1,545	192	192	30	1
Encephalitis, acute	1	1		0		0	0		0	
Enteric fever:										
Typhoid	2	0	0	0		2	0	0	0	2
Paratyphoid	11	1	0	0		0	0	0	0	72 (B)
Food-poisoning	148	13	6	0		188	17	20	0	
Infective enteritis or diarrhoea under 2 years				6	28				11	13
Measles*	24,951	1419	868	584	988	4,618	153	105	26	30
Meningococcal infection	35	4	21	0		35	0	11	0	
Ophthalmia neonatorum	29	10	6	0		26	1	14	0	
Pneumonia†	2,926	276	762	26	16	793	54	338	11	43
Poliomyelitis, acute:										
Paralytic	7	0	0	0	1	15	2	0	2	2
Non-paralytic	2	0	0			10	0			
Puerperal fever§	309	41	22	0		224	31	6	0	
Scarlet fever	1,207	55	78	35	20	853	53	82	23	13
Tuberculosis:										
Respiratory	476	61	87	13		537	69	96	20	
Non-respiratory	53	8	12	6		58	3	10	1	
Whooping-cough	589	23	51	77	117	645	31	49	4	14

DEATHS	1959 Eng. & Wales	1959 Lond.	1959 Scot.	1959 N. Ire.	1959 Eire	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	2	0		0		3	1		0	
Encephalitis, acute		0			0		0			
Enteric fever	1	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	10	0	3	0	0	6	0	3	1	0
Influenza	1,571	163	57	4	4	100	4	3	0	2
Measles		0	0	0	2		0	0	0	0
Meningococcal infection		1	1				0	0		
Pneumonia	2,121	244	95	21	18	819	67	29	17	10
Poliomyelitis, acute	0	0		0	0	1	1		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	143	15	16	1	2	88	12	15	2	5
Non-respiratory		1	0	0	1		1	0	0	3
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0–1 year	410	38	39	13	17	388	34	33	5	18
Deaths (excluding stillbirths)	17,340	1717	1028	161	213	11,524	953	718	155	241
LIVE BIRTHS	15,593	1272	1014	265	373	14,725	1227	1029	229	343
STILLBIRTHS	327	21	25			332	31	25		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Edinburgh University.—A special graduation ceremony will be held on July 21 in connexion with the joint annual meeting in Edinburgh of the British and Canadian Medical Associations. Honorary doctorates in law at the University will be conferred on Lord ADRIAN, O.M., F.R.S., chancellor of Leicester University, Master of Trinity College, B.M.A. gold medallist; Dr. A. MACRAE, secretary of the British Medical Association from 1950 to 1958; Sir ARTHUR PEREGRINE THOMSON, professor of therapeutics and dean of the faculty of medicine, Birmingham University, president of the B.M.A.; Professor C. H. BEST, F.R.S., professor of physiology and head of the department, Toronto University, since 1929; Professor J. RENAUD LEMIEUX, professor of clinical medicine, Laval University, past president of the Canadian Medical Association; and Professor W. G. PENFIELD, O.M., F.R.S., professor of neurology and neurosurgery, McGill University, from 1934 to 1954.

B.M.A. Divisions' TV Symposium.—The North Middlesex and Enfield and Potters Bar Divisions of the British Medical Association held a joint symposium of surgical and clinical procedures on closed-circuit colour television on the evenings of March 9, 10, 11, and 12. The programmes were televised in the North Middlesex Hospital and presented by members of the staff of the hospital and other members of the Divisions. The panels of commentators included Sir RUSSELL BROCK, Sir ERIC RICHES, Professor T. RUSSELL FRASER, Dr. PAUL WOOD, and Dr. A. W. SPENCE. In his opening remarks Dr. N. R. SHERIDAN, honorary secretary of the North Middlesex Division, told the audience that it was a memorable occasion, as it was the first time that such a programme had been presented on a divisional level, previous television demonstrations having been given before national bodies. On each of the four nights there was an audience of over 400 doctors. The meeting was a great success, and the gratitude of all who saw it, and took part in it, is due to Smith, Kline, and French, Ltd., for putting these facilities at the disposal of the medical profession.

Medical Society of London.—The company attending the 179th anniversary dinner of the Medical Society of London at the Park Lane Hotel last week enjoyed some notably urbane oratory. Lord COHEN OF WALMER showed a close acquaintance with the life and works of Lettsom when proposing the toast of the society. As chairman of the Council on Prices, Productivity, and Income, Lord Cohen spoke with authority when he voiced his doubts on whether enough was being spent on the rebuilding of obsolete hospitals. He mentioned the tremendous burden on the medical and administrative staff of hospitals, but thought that too many people were busying themselves writing too many circulars. Dr. E. R. CULLINAN, the president of the society, concluded his entertaining reply by presenting Lord Cohen with a wine-glass made about the same time as the society was founded. Dr. J. B. HARMAN'S speech proposing the health of the guests deserved the compliment paid to it by Professor ANDREW CLAYE, whose reply was in verse.

Optional Latin.—A resolution will be submitted to the Congregation of Oxford University of May 5 which seeks to make Latin an optional instead of a compulsory subject in Responsions, the qualifying examination to Oxford University. The resolution proposes that, in future, candidates for Responsions should be required to pass in two languages in addition to English, one of which shall be chosen from Latin, Greek, German, and Russian. Signatories to the resolution include Dame JANET VAUGHAN, principal of Somerville College, Sir GEORGE PICKERING, regius professor of medicine, and Sir HOWARD FLOREY, F.R.S., professor of pathology. The Senate of Cambridge University announced last month that they were shortly to discuss the best method of retaining Latin and Greek among the subjects for university entrance while abolishing their compulsory nature.

Improved Child Guidance.—In a circular sent to local education authorities on March 11, Mr. GEOFFREY LLOYD, Minister of Education, said that he was in general agreement with the recommendations on child guidance of the Committee on Maladjusted Children, whose report was published in 1955. His aim is a comprehensive child-guidance service in every area, including clinics at which treatment can be given by psychiatrists, psychologists, and psychiatric social workers. Local education authorities and regional hospital boards are asked to plan these clinics in consultation, though it is accepted that development will depend on the availability of trained staff. The Minister also called for wider facilities for the special educational treatment of maladjusted children, who, wherever possible, should live at home and attend an ordinary school.

Mental Health Research Fund.—News was given of the research projects supported by the Fund during the year October 1, 1957, to September 30, 1958, at the annual general meeting on March 18. These projects included a sociological study of the family structure of mental hospital patients, an investigation into the possible biochemical abnormalities in patients suffering from depressive illness, research on childhood psychosis, and an investigation into the character of intellectual disintegration in senile dementia. Funds were also provided to help in the establishment of an animal behaviour research laboratory, and for the study of psychiatric treatment in psychosomatic disorder.

Doctors and the F.B.I.—Recent advertisements inserted by the Federal Bureau of Investigation in the *Journal of the American Medical Association* asking for the co-operation of any doctor who might have seen certain wanted people have started a lively correspondence in *J.A.M.A.'s* columns on whether or not such co-operation would violate the nature of the relationship between a doctor and his patient. The person mentioned in the issue of November 8, 1958, was alleged to have murdered a police officer and was considered to be "extremely dangerous." He was accompanied by a woman who had used drugs which in some States required a doctor's prescription. A month or so later in the December 20 issue another wanted man was alleged to have violated the bankruptcy laws, and was possibly under treatment for a tumour. In the letter which started the controversy, Dr. Manfred S. Guttmacher, of Baltimore, protested against the editorial policy of the *J.A.M.A.* which "permits the F.B.I. to use it as a vehicle for catching criminals." If the present policy were continued, said Dr. Guttmacher, the physician's examination room would resemble a rural post-office, with its walls plastered with photographs of wanted criminals.

Sir Lionel Whitby Medal.—Sir LIONEL WHITBY, late Master of Downing College and regius professor of physic, is to be commemorated in the Cambridge Medical School by a medal to be awarded annually for an M.D. thesis of exceptional merit dealing with investigation carried out in the laboratory, preferably upon a haematological subject. The medal will be endowed by Lady Whitby and her family.

Royal College of Surgeons, England.—At a meeting of the Council on March 12, Mr. G. H. MACNAB (Westminster Hospital) was admitted to the Court of Examiners, and Mr. GORDON PAUL, of Bristol, to the Fellowship *ad eundem*. The Hallett Prize was presented to G. R. DUNCAN, of the University of Otago, New Zealand, and the Handcock Prize to J. C. BULL, of Guy's Hospital Medical School.

College of General Practitioners' Prize.—The College is offering to senior medical students six Public Welfare Foundation Prizes of £40 each for a case history, with a suitable commentary, of one or more patients whom they have seen in general practice. Details and application forms from the Secretary of the College, 41, Cadogan Gardens, London, S.W.3. The closing date is August 1.

Langley Memorial Prize.—A prize of about £21 is offered for an essay on certain aspects of tropical medicine. It is open to officers, past and present, of the West African Medical Departments. Details from the Registrar, London School of Hygiene and Tropical Medicine, Keppel Street (Gower Street), London, W.C.1. Closing date October 1.

Family Planning Association.—The president, Sir RUSSELL BRAIN, received the guests at a reception of the Association at the Royal Commonwealth Society on March 11. The Association's film *Birthright* was shown, and a report on last month's international population conference at Delhi was given by Sir Julian Huxley, F.R.S., Dr. A. S. Parkes, F.R.S., and Mrs. Margaret Pyke.

Polio Vaccine.—Messrs. Pfizer Ltd. announced last week that they had begun production of Salk-type polio vaccine in Britain. One batch of 163,000 doses had passed tests of safety and potency. The chairman stated at a press conference that the type-1 strain being used was Brunenders. He also said that the plant could be used for the production of a live attenuated vaccine if necessary.

Sir Paul Fildes, F.R.S., formerly director of the Medical Research Council's unit for bacteriological chemistry, will receive the honorary degree of D.Sc. of Reading University at a Congregation on May 9.

Faculty of Anaesthetists.—Dr. R. P. W. SHACKLETON, of Southampton, and Dr. B. L. S. MURTAGH, of Birmingham, Fellows in the Faculty of Anaesthetists, have been elected members of the board of the Faculty of Anaesthetists for eight years.

Mr. T. M. Prossor has been appointed by the Army Council as honorary consultant in radiotherapeutics to the Queen Alexandra Military Hospital, Millbank, with effect from March 6.

Professor A. B. Semple, professor of public health, and medical officer of health for Liverpool, is to be a member of the subcommittee appointed by the Central Housing Advisory Committee to consider the standards of design and equipment applicable to family dwellings and other forms of residential accommodation.

Dr. Hossein Samirad, rector of Meshed University, Iran, has arrived in London for a two-weeks visit at the invitation of the British Council.

COMING EVENTS

Society of Chemical Industry.—An exhibition of new laboratory apparatus and techniques will be held in the chemistry department, Birkbeck College, Malet Street, London, W.C.1, at 4 p.m., March 24.

Congrès International de la Neutralité de la Médecine en Temps de Guerre.—This congress, which was postponed in June last year, will now take place from April 6 to 8. Details from CHARLES RICHET, the President, Comité de la Neutralité de la Médecine en Temps de Guerre, 37, rue de Bellechasse, Paris, 7.

Royal Statistical Society.—The Medical Section of the Society will hold a day conference on "Accidents" and "Medical Genetics" at Bedford College, London, on April 17. Speakers will be Dr. F. GARWOOD (child road accidents), Dr. J. P. BULL (types and severities of accidental injuries), Professor G. C. DREW (alcohol and accidents), Dr. T. C. CARTER (the genetical aspects of radiation), and Dr. ELIOT SLATER (the genetics of schizophrenia). Further details from J. A. HEADY, M.R.C. Social Medicine Research Unit, London Hospital Research Laboratories, Ashfield Street, London, E.1. Applications by April 8.

Ileostomy Association of Great Britain.—A divisional general meeting will be held at 2.15 p.m., April 11, at the Birmingham Medical Institute, 36, Harbourne Road, Edgbaston, Birmingham, 15.

Symposium on "The Staphylococcus."—This symposium for consultant pathologists will be held at the Postgraduate Medical School of London, Ducane Road, London W.12, from July 15 to 17. Applications by June 17. Details from the Dean, Postgraduate Medical School. See also advertisement at p. 52 of this week's *Journal*.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 23

BRITISH ASSOCIATION OF SPORT AND MEDICINE.—At Guy's Hospital Medical School (Anatomical Theatre), London Bridge, S.E., 5.30 p.m., Dr. J. Joseph: Anatomy of Movement in Relation to Athletics.

MANCHESTER MEDICAL SOCIETY: SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 5 p.m., Mr. W. G. Cross: Treatment of the Periodontal Pocket.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Ophthalmology Lecture by Professor A. Sorsby: Irregularly Dominant Affections of the Retina.

Wednesday, March 25

BRITISH PSYCHOLOGICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Mr. Michael Reed, B.Sc.: Communication and the Deaf.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Neoplasms of the Kidneys.

MANCHESTER MEDICAL SOCIETY: (1) SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University, 5 p.m., Dr. K. Shirley Smith: Recurrent Angina Independent of Effort. (2) SECTION OF GENERAL PRACTICE.—At Grand Hotel, 8 p.m., Mr. P. W. H. Revington: The Plaintiff was a Patient.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—Physiology Theatre, Gower Street, W.C., 5.30 p.m., public lecture by Dr. Valy Menkin (Philadelphia): Role of Inflammation in Carcinogenesis.

APPOINTMENTS

JACKSON, A. D. M., M.D., M.R.C.P., D.C.H., Part-time Consultant to Children's Department, the London Hospital, London, E.

MCWILLIAMS, L. F., M.B., B.Ch., D.P.H., Medical Officer of Health, Boroughs of Rochester and Chatham.

NAVIN, W. P., M.B., B.Ch., Coventry City Police Medical Officer.

REID, J. J. A., T.D., M.B., Ch.B., B.Sc., D.P.H., Deputy County Medical Officer and Deputy Principal School Medical Officer of Northamptonshire.

ROBERTS, D. P. WYNN, M.B., Ch.B., D.P.H., D.Obst.R.C.O.G., Deputy Medical Officer of Health for Blackpool.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—T. S.-B. Kelly, M.B., Ch.B., F.R.C.S.Ed., D.O.M.S., Consultant Ophthalmic Surgeon in Bath Clinical Area; P. N. Tandon, M.B., B.S., Ear, Nose, and Throat Registrar at South Devon and East Cornwall Hospital, Plymouth; Margaret F. Beard, M.B., B.Chir., Anaesthetic Registrar in Bath Group of Hospitals; B. A. Poley, M.B., Ch.B., D.A., Registrar in Anaesthetics, Southmead Hospital, Bristol; R. H. Harris, M.B., B.S., D.P.M., Assistant Psychiatrist at Digby-Wonford Hospital, Exeter; J. M. Pencheon, M.B., Ch.B., D.P.M., Consultant Psychiatrist in West Cornwall Clinical Area; W. Rodger, M.B., B.Chir., D.P.M., Consultant Psychiatrist in Exeter Clinical Area; A. K. Mitra, M.B., B.S., Registrar in Department of Pathology at Frenchay Hospital, Bristol; E. R. Johns, M.B., B.S., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology at Camborne-Redruth Miners' and District Hospital, Redruth.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Longstaff.—On February 18, 1959, at Felton, Northumberland, to Drs. Peggy and John Longstaff, a brother for Fiona and Siân—William John.

Werry.—On March 6, 1959, at Royal Victoria Hospital, Montreal, Canada, to Jocelyn and John Werry, a son.

DEATHS

Atmore.—On February 25, 1959, at Otaki, New Zealand, Emma Gertrude Atmore (formerly Applegate), M.B., Ch.B., aged 64.

Bowes.—On March 2, 1959, in hospital, Carlisle, Joseph Edward Bowes, M.B., C.M., of Grange-in-Borrowdale, Keswick, Cumberland, aged 92.

Bull.—On March 2, 1958, in hospital, George Vernon Bull, M.B., of White Gables, Sandhurst, Kent, aged 86.

Hamill.—On March 4, 1959, Philip Hamill, M.D., D.Sc., F.R.C.P., of 11, County Gate, London, S.E.

Hole.—On March 5, 1959, at the Royal Naval Hospital, Plymouth, Devon, Kenneth Hill Hole, O.B.E., M.B., B.S., Surgeon Captain, R.N. (retired), of 4, Upper Knollys Terrace, Plymouth.

Lever.—On March 6, 1959, Charles Arthur Ashton Lever, L.R.C.P.&S.I. & L.M., of Brendon House, Llandudno, Caerns, aged 83.

Leyton.—On March 1, 1959, at Brownheath House, Droitwich, Worcs, Helen Gertrude Leyton, M.D.

McKenzie.—On March 7, 1959, Ivy McKenzie, M.D., F.R.F.P.S., of Glasgow, aged 81.

Macmillan.—On March 7, 1959, at Bangour Hospital, John Cairns Macmillan, M.B., Ch.B., of Kinloch Crag, Bo'ness, West Lothian.

Marshall.—On March 4, 1959, at Yatesbury, Tyler Hill, Canterbury, Kent, William Henry Marshall, M.B., formerly of East Grinstead, Sussex.

Somerville.—On March 3, 1959, Hugh Somerville, M.B., Ch.B., D.P.H., of 44, Grange Road, Fenham, Newcastle upon Tyne.

Taylor.—On March 2, 1959, at St. Thomas's Hospital, Hydestile, near Godalming, Surrey, William Benjamin Batchelor Taylor, M.D., D.P.H., F.R.C.S.Ed., of Friday's Hill Cottage, Fernhurst, Haslemere, Surrey, formerly of 35, Connaught Square, London, W., aged 81.

Wassermann.—On February 28, 1959, Dr. Sigmund Wassermann, of Utopia, Parkway, Flushing, New York, U.S.A., aged 69.

Wilson.—On March 4, 1959, at Edinburgh, Charles Wilson, M.B., C.M., of 77, Cluny Gardens, Edinburgh, late of Wallasey, Cheshire.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Storage Life of Drugs

Q.—*How long do drugs keep? One expects tinctures, spirits, etc., to be usable after years, but what about liquid extracts, solutions, syrups, oils, etc.?*

A.—The question of the storage life of drugs and their preparations is a most important one in pharmacy, and many of the *B.P.* and *B.P.C.* monographs have storage conditions specified. A safe rule is to ensure that all preparations are stored in well-sealed containers. This is particularly important with hygroscopic, effervescent, and volatile substances. Even tinctures are liable to lose alcohol, and become more concentrated if allowed to evaporate. Oils, on exposure to air, may become rancid—for example, olive oil—or lose vitamin content—for example, cod-liver oil. Many drugs are inactivated by exposure to light and must be stored in dark bottles—cod-liver oil, adrenaline solution, and paraldehyde are examples. Extracts, with the exceptions of the liquid extracts of ergot and of liver, are usually fairly stable.

Syrups are also generally stable, because the osmotic pressure of their sucrose content as a rule prevents mould or bacterial growth. Occasionally, however, water evaporates from the syrup and forms droplets on the upper part of the bottle. These later drop on to the surface of the syrup and form a dilute sugar solution which is liable to fermentation or mould growth. The monographs in the *Extra Pharmacopoeia*[1] give the storage directions for a wide range of drugs, but these are scattered throughout the book. Concise accounts of the preservation of pharmaceutical products appear in *Bentley's Textbook of Pharmaceutics*[2] and *Tutorial Pharmacy*.[3]

REFERENCES

1 *The Extra Pharmacopoeia, Martindale*. 1958, 24th ed., vol. 1. Pharmaceutical Press, London.
2 Davis, H., *Bentley's Textbook of Pharmaceutics*. 1954, 6th ed. Baillière, Tindall and Cox, London.
3 Cooper, J. W., and Gunn, C., *Tutorial Pharmacy*, 1949, 4th ed. Pitman, London.

Diagnosing Scleroderma

Q.—*Is there any way to prove or disprove a diagnosis of scleroderma?*

A.—Scleroderma of the localized type, morphoea, or one of its variants, or lichen sclerosus (white spot disease) is not usually difficult to diagnose clinically or histologically. There is no other form of proof. In systemic sclerosis there is some difficulty in diagnosis and difference of opinion on aetiology. Clinically the picture may range from little more than Raynaud's disease with acrosclerosis to a widespread systemic fibrosis involving all organs and tissues and associated with, perhaps dependent upon, a generalized sclerosing vasculitis. The clinical features and histological appearances are well described. There is no other specific test to prove or disprove the diagnosis.

Tapeworm Infection from Cats

Q.—*If a pet cat has tapeworms, is there any danger to children? Is it safe to add the contents of the sanitary tray containing cats' excreta, possibly infected, to a compost heap which might later be used on vegetable crops?*

A.—Pet cats or dogs which are obviously harbouring tapeworms should be treated with suspicion at all times and with anthelmintics at the earliest opportunity, especially when children are concerned. *Dipylidium caninum* is a common and cosmopolitan tapeworm of dogs and cats and is an occasional parasite of man, who becomes infected with it by swallowing accidentally the intermediate host (flea or louse) which harbours the infective larva (cysticercoid). *Taenia taeniaeformis* is the common and cosmopolitan tapeworm of cats, but has never been found in man. The related species in dogs, *Taenia multiceps*, however, has a larval stage (*Coenurus cerebralis*) which lodges in the central nervous system of sheep, goats, etc., and sometimes in that of man.

On principle, therefore, any kind of *Taenia* infection in cats and dogs should be removed, since their eggs, if swallowed, *may* be a potential source of danger to human beings. The addition of cats' excreta to a compost heap is a safe method of disposal, as the heat generated in the heap should kill the eggs.

Onion for Wasp-sting

Q.—*Is sucking an onion as a remedy for a wasp-sting of the tongue nonsense or sound treatment?*

A.—This remedy is well known to the laity. The venom apparatus of the wasp consists of the sting, the venom sac and glands, plus Dufour's alkaline gland. In so far as the reaction of an onion is acid and the secretion of Dufour's gland is alkaline, sucking an onion might help. However, wasp venom contains histamine, 5-hydroxytryptamine,[1] and "kinin,"[2] and it appears unlikely that an onion would neutralize these substances.

REFERENCES

1 Jaques, R., and Schachter, M., *Brit. J. Pharmacol.*, 1954, 9, 53.
2 Schachter, M., and Thain, E. M., ibid., 1954, 9, 352.

Hormones in Seminal Fluid

Q.—*To what extent are the hormone constituents of seminal fluid absorbed through the vaginal mucosa, and what effect have they on the female?*

A.—Small amounts of oestrogen and androgen have been detected in seminal fluid, and there is some experimental evidence that absorption of the oestrogen through the vaginal mucosa in immature rabbits hastens the maturation of the uterus. There is no convincing evidence that such an effect exists in the human female, though the possibility has been inferred from the experimental results mentioned above. The possibility has, in fact, been used as an argument against the use of a condom during intercourse in newly married couples, since it has been suggested that the wife's fertility may thereby be impaired. There is no factual evidence to support such a possibility.

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